A FIVE YEAR RETROSPECTIVE HISTOPATHOLOGIC STUDY ON SALAIVARY GLAND LESIONS

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CERTIFICATE

We hereby certify that the work embodied in the dissertation entitled **"A Five Year Retrospective Histopathologic Study On Salaivary Gland Lesions"** is a record of work done by **Dr. J. Latha** in the Department of pathology, Tirunelveli Medical College, Tirunelvelli. During her Post Graduate Degree course in the period 2009 – 2012. This work has not previously formed the basis for the award of my degree or diploma.

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INTRODUCTION

Salivary glands are one of the important exocrine glands. They are classified according to size as major (eg. Parotid, Submandibular and sublingual) and minor (eg. Lip, mounth and throat) glands. Their secretion may be serous, mucous or mixed. Saliva secreted from these glands keeps the oral mucosa moist and carbohydrate digestion starts in the mouth by ptyalin.

Salivary gland lesions range from inflammation to neoplasm. Salivary gland lesions constitute 2.68% of oral mucosal lesions, Sajeevan et al (2003). The salivary glands are the site of origin of a wide variety of neoplasms. The histopathology of these tumours in said to be the most complex and diverse of any organ in the body. Salivary gland neoplasm are also relatively uncommon and they constitute about 3% of all head and neck neoplasms. About 80% of tumours located in parotid gland, 10-20% in submandibular gland and several percentage in sublingual and minor salivary gland ,Wierzbicka et al(2010). Benign neoplasm make up about 80% of parotid tumours, 50% of submandibular tumours and less than 40% of sublingual and Minor salivary gland tumours ,Eisele et al (2001).

AIMS AND OBJECTIVES

The aim of the study is to

1. Record the incidence of salivary gland lesions reported to Tirunelveli Medical College Hospital.
2. Classify the lesions into inflammatory, neoplastic and others.
3. Categorise the neoplastic lesions as per the WHO classification.
4. Compare and analyze our data with similar studies .

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REVIEW OF LITERATURE
SALIVARY GLAND LESION

Salivary gland structure

There are three major paired salivary glands (parotid, submandibular, sublingual) and numerous minor salivary glands (submucosa of the upper aerodigestive tract i.e. lips and nasal cavity to major bronchi). These exocrine glands secrete components of saliva that lubricate the food and breakdown carbohydrates.

Macroscopic

Parotid glands composed of a superficial lobe and deeper smaller lobe and facial nerve runs between the two lobes. Each gland contains about 20 intraglandular lymphnodes. Most salivary gland tumors arise from the superficial lobe and present as facial swellings. Tumors that occur in the deep lobe often expand through the parapharyngeal space, manifesting as pharyngeal swelling, Kaplan M and Johns M (1993). The accessory lobe of the parotid gland, situated adjacent to Stenson's duct and separate from the main body of the parotid gland, is found in 21% of normal subjects, Frommer J et al (1977). Tumors arising in this lobe often present as midcheek masses, Lin D T et al (2004). Parotid secrete serous fluid and empty into oral cavity near second maxillary molar via Stensen's duct.

Submandibular (submaxillary) glands secrete serous and mucous fluids and empty at floor of the mouth through Wharton's duct.

Sublingual glands secrete serous and mucous fluid, partly empty at floor of the mouth through Bartholin's duct directly and partly coalesce to empty into Wharton's duct. Both the Bartholin's duct and Wharton's duct open in the floor of the mouth on either side of the tongue frenulum. Minor salivary glands can be found in the lateral margins of the tongue, lips, buccal mucosa, palate, and glossopharyngeal area. Among them, the palate is the site of predilection for salivary gland neoplasms. The minor glands are seromucinous or predominantly mucous, depending on location.

Microscopic

Major glands are enclosed by connective tissue capsule and divided into lobules composed of ducts and acini. Minor salivary glands are not capsulated. Preservation of the lobular architecture is an important feature favoring a diagnosis of a non-neoplastic process over a tumor. The entire glandular structure is a two-tiered organization which comprises luminal (acinar and ductal cells) and abluminal (myoepithelial and basal cells). The acini are lined by epithelial cells surrounded by myoepihelial cells which lie between acinar cell and basement membrane. The striated ducts and the downstream conducting units are lined by simple or pseudostratified columnar epithelium which gradually transforms into stratified squamous epithelium in the salivary duct, as they reach the oral epithelium and they are supported by basal cells.

The acinar portion of all Salivary glands are composed of either serous or mucinous cells. Serous cells are pyramidal in shape contain periodic acid schiff (PAS) positive and mucicarmine negative granules within their cytoplasm and large basel nucleus. Mucous cells are rounder cuboidal to columnar with small basally oriented nuclei and finely vacuolated cytoplasm containing sialomucins. They are PAS-positive and mucicarmine positive. The luminal cells of the intercalated ducts are cuboidal, with eosinophilic to amphophilic cytoplasm and centrally located nuclei. The striated ducts are lined by columnar cells with granular cytoplasm which are mitochondria rich and subnuclear vertical striations due to the prominent basal folds in the plasma membrane. The luminal cells are readily highlighted by immunostaining for cytokeratin, carcinoembryonic antigen (CEA), and epithelial membrane antigien (EMA).

Myoepithelial cells are physiologically and functionally modified epithelial cells situated between the luminal cells and the basement membrane. They are stellate-shaped with cytoplasmic processes embracing the acini or spindle-shaped surrounding the intercalated ducts.

They possess a dual epithelial and smooth muscle phenotype characterized ultrastructurally by the presence of desmosomes, intermediate filaments, pinocytotic vesicles, and myofilaments, Dardick I (1996). They may also exert an anti-invasive effect in neoplasms by

promoting epithelial differentiation, secreting proteinase inhibitors, and suppressing angiogenesis, Savera A T and Zarbo R J (2004).

The abluminal cells in the striated ducts, excretory ducts, and salivary ducts are basal cells, which differ ultrastructurally from myoepithelial cells in the absence of myofilaments. They play an important role in the processes of regeneration and metaplastic changes, Ihrler S et al (2002). Oncocytic cells, seen after 50 years of age replaces the normal cells of ductoacinar units. Oncocytic metaplasia has been implicated in the development of oncocytic hyperplasia, nodular oncocytosis, and even oncocytoma, Krech R et al (1981).

Epidemiology

The distribution of salivary gland lesions were recorded almost all parts of the world. But the incidence level varies for different parts of the world. The different level of salivary gland lesions occured were 2.68% of oral lesions in northern Tamilnadu, Sajeevan et al (2003), 141 per 8 years in Malaysia, Jayaram and Dashini (2011), 185 per 3 years in West Bengal, Bandyopadhyay et al (2005), 3.5% of head and neck tumour over 21 years in Nigeria, Kolude et al (2001), 1.9% of total cases over 41 years in Thailand, Dhanuthai et al (2009), 0.15% of total cases over 20 years in Portuguese, Lima et al (2005).

Sialadenitis

Inflammation of the salivary gland is called sialadenitis. It may be due to the following reasons.

- Mechanical – obstruction
- Physical - Radiation, Seifert G et al (1986)
- Infections :
  - Bacterial (staphylococcus aureus, streptococci – acute suppurative sialadenitis). Clinical signs include tender, diffuse or localized swelling that may fluctuate, later fistula draining purulent material may form (Seifert G et al., 1986). Microscopically edema, hyperemia and acute inflammation and periductal or intraductal accumulation of neutrophils and destruction of ductal epithelium. Acini lost and paranchymal microabscesses form.
  - Viral - Paramyxo in mumps, Coxsackie, EpsteinBarr, Influenza A (Seifert G et al.,1986). Mumps clinically swollen and painful. Microscopically dense interstitial lymphoplasmocytic infiltrate, acinar cell vacuolization and ductal dilatation, Seifert G et al (1986); Hanson D et al (1971).
- Autoimmune - Sjogren syndrome, Rheumatoid arthritis, Hyper gammaglobulinemia. Early stage there is lymphoplasmocytic septal inflammatory infiltrate. Sever stage extensive lymphoid infiltrate with germinal centers, acini atrophic, interstitial fibrosis. In late stages acini are absent and ducts with intraepithelial lymphocytes, Bloch KS et al (1965).

Chronic sialadenitis

The causes for chronic sialadenitis are Sialolithiasis, Autoimmune, Radiation therapy and duct strictures. Grossly there is hard, fibrotic gland. Microscopically in early stage dilated ducts filled with secretions & lymphoplasmacytic infiltrate. Later stage fibrosis around duct & lobulation of gland with acinar atrophy. Differential diagnosis include lymphoepithelial lesion or Warthin's tumor in which epithelial component present in both condition. Treatment is surgical removal.

Sialolithiasis

Various calcified masses that form in the ducts of salivary glands. They form from the calcification of an intraluminal organic nidus such as a dried secretion, bacterial colonies or cellular debris. Their exact cause is not known, but inflammation of the salivary duct and the viscosity and stasis of saliva have been suggested as predisposing factors, Koudelka BM (1991); Shafer WG et al (1983). The stones are predominantly composed of calcium phosphate in the form of hydroxyapatite, Anneroth G et al (1975).

Clinical signs include distention of the duct, swelling and pain. Grossly there is round or oval stone with smooth or rough surface, colour varying from white to yellow. Microscopically duct epithelium is compressed and may show squamous, oncocytic or mucous cell metaplasia. Recurrent infection and retention of secretions lead to parenchymal atrophy and scarring of the gland. Diagnosis can be made by

radiological imaging studies and the treatment is removal of the stone and affected portion of the gland.

Mucoceles

Pooling of mucin in a cystic cavity is called mucocele. The two types of mucoceles are retention type in which mucin in dilated duct and extravasation type where mucin accumulates in soft tissue. Common sites affected are lower lip, tongue, floor of the mouth (ranula) and buccal mucosa and incidence is more in the third decade of life.

Grossly cystic cavity in the connective tissue filled with glistening fluid. Microscopically cyst wall may or may not contain epithelial lining. The retention type has lining and no surrounding inflammation. In extravasation type there is mucin with surrounding inflammatory cells and no lining seen, there will be foamy histiocytes. Treatment for mucocele is surgical excision.

Benign lymphoepithelial cysts

Benign lymphoepithelial cysts are unifocal lesions and seen in fifth and sixth decades of life. These cysts are unilateral and always occur in parotid gland, sometimes oral cavity is affected. Grossly well circumscribed unilobular cysts with serous to mucoid to caseous and keratinous debris may present.

Microscopically cyst is seen lined by benign mature squamous epithelium without papillary projections, rarely cuboidal or columnar with goblet cells. Below the epithelium, the cyst wall has dense lymphoid

tissue with germinal centers. The treatment for benign lymphoepithelial cyst is excision of the cysts.

NEOPLASMS

The worldwide annual incidence of salivary gland tumors ranges from 0.4 to 13.5 cases per 100 000 people, Auclair P L et al (1991). In general, salivary gland tumors are most common in older adults and females are more commonly affected than males, except for Warthin tumor and high-grade carcinomas. Epithelial tumors constitute 80-90% of all salivary gland tumors, with the majority being benign (75%), and pleomorphic adenoma is the commonest (about 65% of all tumors). The parotid gland is the commonest site for occurrence of salivary gland tumors.

Primary carcinomas of the salivary glands are uncommon, accounting for fewer than 0.3% of all cancers. The sites of occurrence with respect to the number of cases in descending order are: parotid gland, submandibular gland, palate, cheek, and tongue. However, tumors have the highest chance of being malignant if they arise from the retromolar area (89.7%), floor of mouth (88.2%), tongue (85.7%), and sublingual gland (70.2%), Ellis G L et al (1991), while only approximately 20% of all parotid tumors are malignant. Among the salivary gland carcinomas, the commonest histologic types in descending order are: mucoepidermoid carcinoma, adenoid cystic carcinoma, adeno-carcinoma not otherwise specified (NOS) and acinic cell carcinoma, with

polymorphous low-grade adenocarcinoma (PLGA) replacing adenocarcinoma NOS in the minor salivary glands, Kokemueller H et al (2004); Wahlberg P et al (2002).

Facial nerve paralysis is a more consistent sign of malignancy, more often seen in high-grade tumors such as squamous cell carcinoma and undifferentiated carcinoma, although it can also rarely occur in Warthin tumor and Pleomorphic adenoma, Seifert G et al (1986). In patients under the age of 18, half of the epithelial tumors are malignant, with low-grade mucoepidermoid carcinoma being the commonest, Seifert G et al (1986); Da Cruz Perez D E et al (2004).

Some salivary gland carcinoma are biologically low-grade (eg. acinic cell carcinoma, PLGA, basal cell adenocarcinoma, epithelial-myoepithelial carcinoma, clear cell carcinoma, cystadenocarcinoma) and some are biologically high-grade (eg. salivary duct carcinoma, most cases of carcinoma, ex pleomorphic adenoma, undifferentiated carcinoma, oncocytic carcinoma)

Rare salivary gland tumors show hybrid features. Hybrid tumor refers to a tumor that is composed of two or more histologically distinct components at a single site, Seifert G et at (1996). The most common components of hybrid carcinomas are salivary duct carcinoma, epithelial-myoepithelial carcinoma, and adenoid cystic carcinoma, Seifert G et at (1996); Ruiz-Godoy L M et al (2003). Others include mucoepidermoid carcinoma, acinic cell carcinoma, squamous cell carcinoma, basal cell adenocarcinoma, and PLGA, Seifert G and Donath K(1996); Zardawi I M

et al (2000). Treatment is probably best based on the histologic component with higher-grade malignancy, Ruiz-Godoy L M et al (2003).

The tumours are classified based on differentiation of components of salivary gland (aciner cell, myoepithelial cell or ductal cell) as follows

WHO Histological Classification of Tumors of the Salivary Glands, Eveson et al (2005)	
Malignant epithelial tumors	**Benign epithelial tumors**
Acinic cell carcinoma	Pleomorphic adenoma
Mucoepidermoid carcinoma	Myoepithelioma
Adenoid cystic carcinoma	Basal cell adenoma
Polymorphous low-grade adenocarcinoma	Warthin's tumor
	Oncocytoma
Epithelial-myoepithelial carcinoma	Canalicular adenoma
	Sebaceous adenoma
Clear cell carcinoma, not otherwise specified	Lymphadenoma
	Sebaceous
Basal cell adenocarcinoma	Non-sebaceous
Sebaceous carcinoma	Ductal papillomas
Sebaceous lymphadenocarcinoma	Inverted ductal papilloma
	Intraductal papilloma
Cystadenocarcinoma	Sialadenoma papilliferum
Low-grade cribriform cystadenocarcinoma	Cystadenoma
	Soft tissue tumors
Mucinous adenocarcinoma	Hemangioma
Oncocytic carcinoma	**Hematolymphoid tumors**
Salivary duct carcinoma	Hodgkin's lymphoma
Adenocarcinoma, not otherwise specified	Diffuse large B-cell lymphoma
Myoepithelial carcinoma	Extranodal marginal zone B-cell lymphoma
Carcinoma ex pleomorphic adenoma	**Secondary tumors**
Carcinosarcoma	
Metastasizing pleomorphic adenoma	
Squamous cell carcinoma	
Small cell carcinoma	
Large cell carcinoma	
Lymphoepithelial carcinoma	
Sialoblastoma	

According to the incidence, most common salivary gland tumours are

Histologic Classification and Incidence of Benign and Malignant Tumors of the Salivary Glands, Ellis et al (1996).	
Benign	**Malignant**
Pleomorphic adenoma (50%) (mixed tumor) Warthin tumor (5% to 10%) Oncocytoma (1%) Other adenomas (5% to 10%) Basal cell adenoma Canalicular adenoma Ductal Papillomas	Mucoepidermoid carcinoma (15%) Adenocarcinoma (NOS) (10%) Acinic cell carcinoma (5%) Adenoid cystic carcinoma (5%) Malignant mixed tumor (3% to 5%) Squamous cell carcinoma (1%) Other carcinomas (2%)

Benign neoplasms

Pleomorphic adenoma

Pleomorphic adenoma is the most common salivary gland tumour. The glands mostly affected are parotid gland, hard palate and submandibular gland. Pleomorphic adenoma occurs more frequently in women then men, and is most prevalent from the fourth to sixth decades, with a mean age of 45 years. It usually presents as a slow growing and painless swelling. When it occurs in the minor glands, ulceration of the

overlying mucosa or apparent fixation to surrounding tissue can be seen rarely. Pleomorphic adenoma can occur in various mucosal sites such as nasal cavity, bronchus, skin (also known as Chondroid Syringoma of breast, and soft tissues, Badia L et al (1996); Croitoru C M et al (1999).

Pleomorphic adenoma is a benign neoplasm consisting of cells with epithelial (luminal) and myoepithelial (abluminal) differentiation, accompanied by variable amounts of characteristic stroma. The diverse morphology results from amalgamation of cellular and stromal components. The coexistence of apparently epithelial and mesenchymal elements gives rise to the synonym “mixed tumor”. Pleomorphic adenoma is now widely accepted as a pure epithelial tumor with divergent differentiation instead of collision of epithelial and mesenchymal tumors. The monoclonal origin of both epithelial and mesenchymal elements has also been supported by molecular analysis, Noguchi S et al (1996).

Grossly the size ranges from a few millimeters to several centimeters. The tumore is typically thinly encapsulated and solitary. Intraoral examples, especially those arising from the palate, may lack a well-defined capsule. The cut surface may be rubbery, fleshy, mucoid, or glistening, depending on the amount of stroma in the tumor. In areas where the capsule is deficient tumor buds may lie in direct contact with the adjacent salivary tissue, Lam K H et at (1990).

Microscopically there is mixture of epithelial and mesenchymal elements. Epithelial elements contain ductual structure with myoepithelial layer and myoepithelial cells contain spindle, clear, plasmacytoid or basaloid elements. In myxoid type there is >80% mesenchymal tissue, cellular type contain > 80% epithelial tissue and mixed or classic type contain equal mixture of these tissues. Histologic appearance consists of tubular structures enveloped by myoepithelial mantles submerging in a chondromyxoid stroma. The interface between the tumor islands and the stroma is usually poorly demarcated. The myoepithelial mantle radiates centrifugally, forming sheets, clusters, lattices, and isolated cells, where they appear to “melt” into the sea of stroma which they produce.

The luminal cell component takes the form of anastomosing tubules, cysts, ribbons, and solid sheets. The cells may be columnar, cuboidal or flat. The duct lumen may be empty or contain eosinophilic colloid like material, which is PAS-positive diastase-resistant and variably mucicarmine-positive. Rarely, metaplastic change to squamous, sebaceous, oncocytic or clear cells can occur. Myoepithelial or modified myoepithelial cells appear as cuboidal, spindle, stellate, plasmacytoid hyaline, nondescript epithelioid, and hydropic clear cells. The spindle or cuboidal cells surround the ducts in a single layer, thick mantle, or radiating corona. They can form nondescript sheets, trabeculae, and even cribriform structures.

Plasmacytoid hyaline cells represent the most distinctive form of modified myoepithelial cells, they are oval-shaped with homogeneous eosinophilic hyaline cytoplasm. The nucleus is round and eccentrically located, with a tendency for peripheral margination of the dense chromatin. Stellate or spindle myoepithelial cells occur singly, or form anastomosing strands, suspended in an abundant myxoid matrix. Uncommonly, myoepithelial cells may merge into squamous nests or cystic squamous lined structures filled with keratin, suggesting an ability to differentiate towards the squamous lineage. Rarely, skeletal muscle differentiation and scattered melanocytes can occur, the latter also imparting a pigmented macroscopic appearance to the tumour, Lam P W et al (1997); Takeda Y et al (2004).

The main application of immunohistochemistry is to demonstrate the coexistence of glandular and myoepithelial components when the diagnosis is uncertain. The glandular component, which may be inconspicuous, can be highlighted by EMA, CEA, or c-kit. Currently the most reliable markers for the neoplasitc myoepithelial component are p63 and calponin, Bilal H et al (2003).

Pleomorphic adenoma shoule be differentiated from Monomorphic adenoma, Adenoid cystic carcinoma, PLGA, Epithelial-myoepithelial carcinoma, Mucoepiedermoid carcinoma. The treatment of choice is complete surgical excision (with rim of uninvolved tissue). The recurrence rates at 5 and 10 years following complete excision are 3.4%

and 6.3% respectively, Hickman R E et al (1984). Enucleation alone, rupture or spillage of tumor during removal, presence of protuberances beyond the main tumor, abundance of chondromyxoid stroma, and young age are associated with a higher recurrence rate, Laskawi R et al (1998); McGregor A D et al (1988).

Warthin's tumor (papillary cystadenoma lymphomatosum)

It is a second most common salivary tumour, Eneroth (1971); Spiro R H (1986) and occur only in parotid gland. Most common bilateral or multifocal tumor of sixth or seventh decade and associated with smoking and definite male predominance. But now, change is seen probably due to a decline in the smoking habit, an established risk factor for this tumor, in men, and a reverse trend in women, Yoo G H et al (1994). Studies conducted among atomic-bomb survivors suggest that radiation may also be implicated in the tumorogenesis, Saku T et al (1997).

Sudden painful increase in size associated with acute pain (known as papillary cystadenoma lymphomatosum syndrome) has been postulated to be caused by leakage of fluid into the surrounding tissues and retrograde infection from the oral cavity via the Stensen's duct. Rarely, facial nerve palsy may be seen in tumors complicated by inflammation and fibrosis, which may be mistaken clinically or intraoperatively for carcinoma. Warthin tumor is multicentric in 12-20% of patients (either synchronous or metachronous), and bilateral in 5-14%, Maiorano E et al (2002). In addition, serial sectioning may reveal

additional subclinical lesions in 50% of cases. This tumor is sometimes seen in association with other benign salivary gland tumors, especially pleomorphic adenoma, Shikhani L T et al (1993). Grossly soft, brown or yellow mass composed of cyst and the cyst with viscous brown fluid.

Microscopically cystic and/ or papillary epithelium consists of two layers a luminal layer of oncocytic columnar cells supported by a discontinuous layer of oncocytic basal cells. The nuclei of the luminal cells appear uniform and display palisading towards the free surface. Their brightly eosinophilic granular cytoplasm is due to accumulation of mitochondria, Shintaku M et al (1997). The basal cells possess round to oval nuclei and small but conspicuous nucleoli. The lumens of the cysts contain thick proteinaceous secretions, cellular debris, cholesterol crystals, and sometimes laminated bodies that resemble corpora amylacea, David R et al (1978). Epithelium overlies dense, polyclonal lymphoid component forms germinal centers. A distinct layer of basement membrane separates the cyst lining from the lymphoid stroma, which consists of small lymphocytes and some plasma cells, histiocytes, and mast cells, and may show giant cell formation, fibrosis or squamous metaplasia from trauma/cyst rupture or after fine needle aspiration.

Differential diagnosis, typical Warthin tumour has a highly distinctive morphology and poses no problem in diagnosis. It differs from oncocytoma in the presence of a prominent lymphoid component, papillae, and glands rather than trabeculae and packets, and conspicuous

basal cells (which are inconspicuous in the latter tumor). The squamous metaplastic Warthin tumor, particularly if infarcted, can be mistaken for squamous or mucoepidermoid carcinoma. Squamous metaplasia of Warthin tumor usually lacks keratinization, which is seen in most squamous cell carcinomas. In contrast to low-grade mucoepidermoid carcinoma, there is no definite infiltrative growth and the tumor cells appear more frankly squamous.

The treament is surgical excision. Superficial parotidectomy or enucleation of tumor is curative. The rare recurrences (<20%) are believed to represent either a second primary or an expression of multifocal tumour, Ebbs S et al (1986). In old patients or those with poor surgical risk, observation without surgery may be an option.

Basal cell adenoma

It is composed of basaloid cells sharply delineated from the stroma by basement membrane-like material. It usually exhibits a monotonous solid, trabecular, tubular, or membranous growth pattern. It occur in adults and 75% in parotid gland. Clinically, it is asymptomatic and a slow growing mass.

Grossly it presents as solid, well circumscribed and pink to brown cystic tumour. Microscopically the edge of the tumour contain small cell with little cytoplasm, show peripheral palisading and give basaloid appearance. The center of the tumour presents polygonal basaloid cells with slightly more cytoplasm and round to oval nucleus and more open

chromatin.Trabecular of membranous pattern have jig-saw puzzle appearance with rounded nests of tumor shaped like puzzle pieces. Membranous pattern additionally show hyalinized eosinophilic linear or modular basement membrane like material around the nests.

Basal cell adenoma is immunopositive for pan –cytokeratin, S - 100, smooth muscle actin, muscle – specific actin, Bilala H et al (2003); Edwards P C et al (2004); Weber A et al (2002).

Basal cell adenoma should be differentiated from Basal cell adenocarcinoma and Adenoid cystic carcinoma. These two tumours contain infiltrative growth and/or perineural invasion. Simple surgical excision is the treatment of choice. Recurrence is rare except for the membranous type, which is associated with a recurrence rate of 25% because of its multifocal nature. Basal cell adenoma may rarely undergo malignant transformation (carcinoma ex monomorphic adenoma 4%)to basal cell adenocarcinoma, adenoid cystic carcinoma, salivary duct carcinoma, or adenocarcinoma NOS, Nagao T et al (1997) .

Canalicular adenoma

Canalicular adenoma arise from excretory ducts and second most common salivary gland lesion of upper lip and always arise from minor salivary gland and multifocal in nature. Women and African Americans are most affected and peak incidence is in seventh decade of life. It is asymptomatic, fluctuate or firm and presents as submucosal nodule growing slowly usually 1 to 2 cm.

Canalicular adenoma occurs most commonly in the elderly, with a mean age of 65 years and mild female predilection, Ellis G L et al (1996). It is primarily an oral lesion. The upper lip is the site of predilection, which accounts for 74% of the cases, followed by the buccal mucosa (12%), palate, and rarely, major salivary glands. The patients present with a non-ulcerated, painless mass that grows slowly. Infrequently, multifocal nodules, ulceration, necrosis, and bone destruction may be seen. Grossly the tumour is not encapsulated but well circumscribed, Rousseau A et al (1998) and have tan to pink cystic or solid cut surface.

Microscopically long strands or tubules of columnar epithelial cells with loose, collagenous stroma and two rows of columnar cells situated opposite to each other. Strands take beaded appearance with tubules coming together and then separating. Tubule epithelial cells have eosinophilic cytoplasm and range from cuboidal to basaloid. The stroma is characteristically edematous with many capillaries and sinusoids; it can be so loose that tumor strands may appear to be “floating in the air”, Ellis G L et al (1996). Diagnosis the tumor cells are positive for cytokeratin, vimentin, S-100 protein, and, infrequently to EMA, Zarbo R J et al (2000). Treament is simple local excision.

Myoepitheliomas

Myoepithelioma is a benign tumor composed exclusively, or almost exclusively, of neoplastic cells exhibiting myoepithelial differentiation. While some investigators require total absence of ductal

component for this designation, Ellis G L et al (1996) most accept the presence of a minor epithelial component (e.g. less than 5-10%), Dardick I, (1995).

Pleomorphic adenoma, basal cell adenoma, and myo-epithelioma can be envisaged to lie on a continuum: myoepithelioma may represent an extreme form of basal cell adenoma without a ductal component, whereas basal cell adenoma is “pleomorphic adenoma lies in the middle of this continuum, Simpson R H et al (1995).

Myoepithelioma most frequently affects the parotid gland and palate. Less commonly, it can occur in the skin, breast, or soft tissue, Hornick J L et al (2003). Clinically, it presents as a painless mass. The peak age is from the third to fifth decade with no sex predilection, Ellis G L et al (1996); Simpson R H et al (1995). Grossly it is a well circumscribed and encapsulated tumour with tan or white cut surface.

Histologically sheets and cords of tumour cell of 4 types are present.Spindle cell are interlacing with fascicular growth pattern hyaline.Plasmacytoid cells are loosely cohesive myoepithelial cells with eosinophilic cytoplasm and eccentric round nuclei. Clear cell are small tubules lined by single layer of cuboidal cell surrounded by one or more layers of clear cells. First two cell types being most common. Either a single cell type predominates in a tumor, or there can be a mixture of cell types. Myoepitheliomas of the minor glands tend to be composed of plasmacytoid cells, and those of the parotid are more often composed of

spindle or epithelioid cells. The stroma is usually scanty,but variable amounts of myxoid or hyaline stroma can be present. Collagenous crystalloids in the form of radially arranged and intercellular hyaline materials are variably present, Simpson R H et al (1995). All have collegenous or myxoid stroma.

Myoepitheliomas should be differentiated from Pleomorphic adenorma or Basal cell adenoma, Myoepithelial carcinoma and various mesenchymal lesions. Myoepithelioma is positive for S-100 and Cytokeratin, Simpson RH et al (1995) and variably reactive for smooth muscle actin and Glial fibrillary acid protein (GFAP). The prognosis is excellent and recurrence is not expected after complete excision and the treatment is simple excision

Oncocytoma

It is a rare tumour and constitute 2.3% of benign salivary tumors and occur after sixth decade. Site of occurrence is major on parotid, few on submandibular and minor (palate, buccal mucosa) glands. It is a slow growing nontender mass and firm, may be multilobulated, mobile on examination. Oncocytoma most commonly occurs in the parotid gland of older adults without gender predilection, Ellis G L et al (1996); Brandwein M S et al (1991), but the submandibular gland can also be affected. Radiation exposure to the head and neck region has been implicated in the pathogenesis in about 20% of cases; this risk factor is

also associated with presentation 20 year younger than those without a history of irradiation.

Oncocytoma is a discrete, encapsulated tumor consisting exclusively of oncocytes and lacking features of other defined tumor types, Thompson LD et al (1996). Oncocytoma, when accompanied by lymphoid stroma, can be indistinguishable from a Warthin tumor. Alternatively, it has been argued that oncocytoma may represent Warthin tumor that lacks lymphoid stroma. Oncocytosis is a diffuse oncocytic metaplastic process in the salivary gland, often associated with atrophy of the surrounding parenchyma, Palmer T J et al (1990).

The lobular architecture is, however, preserved. Nodular oncocytic hyperplasias consist of multiple nodular proliferations of closely packed oncocytes. The nodules are less circumscribed and organized than those of oncocytoma and a fibrous capsule is lacking, Palmer T J et al (1990); Hartwich RW et al (1990).

Grossly it is homogenous with smooth surface divided into lobules by fibrous tissue. Microscopically sheets, nests or cords of uniform oncocytic cells are large with distinct borders filled with an acidophilic granular cytoplasm and the granularity due to mitochondria (60%). Which can be highlighted by phosphotungstic acid hematoxylin stain or immunostaining with antimitochondrial antibody, Shintaku M et al (1997).

Diagnosis can be done by Phosphotungstic acid hematoxylin, Bensleys aniline acid fuchsin and Luxol- fast-blue reaction. Typical oncocytoma is not difficult to diagnose, but salivary gland tumors with prominent oncocytic change, most notably Warthin tumor, pleomorphic adenoma, basal cell adenoma, and the oncocytic variant of mucoepidermoid carcinoma are pose challenge to diagnose. Nuclei of acinic cell carcinomas are peripherally located, in contrast to the central round nuclei in oncocytoma, Brandwein M S et al (1991). Prognosis is excellent. Surgical excision is the treatment of choice and recurrence is uncommon (0-10%), Brandwein M S et al (1991).

MALIGNANT

Mucoepidermoid carcinoma

Mucoepidermoid carcinoma is a most common malignant tumor in adult and childhood, Ellis GL et al (1996) and composed of mucous, intermediate, epidermoid (or squamoid) cells. The tumor typically presents as a slow-growing painless mass. About one-third of patients experience tenderness, pain, drainage from the ipsilateral ear, dysphagia, and trismus. Facial paralysis is uncommon, except in high-grade tumors, Seifert G et al (1986). Age of presentation spans from the first to the ninth decades, peaking in the fourth decade. There is a slight female predilection. The parotid gland (45%) and palate (21%) are the commonest sites of occurrence, Ellis G L et al (1996).

It is the principal histologic type of radiation-related salivary gland carcinoma in survivors of the atomic bombings of Hiroshima and Nagaski, Saku T et al (1997). This tumor also occurs with increased frequency among children who received high-dose and low-dose radiotherapy for leukemia and tinea capitis respectiviely, Modan B et al (1998).Mucoepidermoid carcinoma has been described in the nasal cavity, paranasal sinuses, nasopharynx, breast, bronchus, thymus, and skin, Nonaka D et al (2004); Shhilo K et al (2005); Riedlinger W F et al (2005). Typically presents as asymptomatic radiolucent lesion. It usually shows low-grade malignant behavior and histology.

Grossly have solid and cystic components and cyst with mucinous material. Microscopically, three cell types are seen as sheets, nests, duct like structures or cysts. Intermediate cells predominate and range from small basal cells with minimal basophilic cytoplasm to large oval cells with pale eosinophilic cytoplasm. Mucin producing cells (Mucocytes) occur singly or as clusters and have pale, foamy cytoplasm, distinct cell membrane and eccentric small nuclei, frequently line cystic spaces and are positive with mucicarmine or PAS stains. Epidermoid or squamoid cells have abundant eosinophilic cytoplasm and vesicular nuclei with open chromatin, not truly squamous they lack intercellular bridges, rarely true keratinization.

The stroma is characteristically sclerotic and abundant, with chronic inflammatory cell infiltration and occasional extravasated mucin

pools. Rarely, there can be a dense lymphoplasmacytic infiltrate admixed with tumor islands, scattered multinucleated giant cells in the stroma, or melanin pigmentation, Auclair P L (1994); Donath K et al (1997). Population of clear cells scattered throughout the tumor, having high glycogen content, can be demonstrated by PAS staining.

Low grade Mucoepidermoid carcinoma have cystic, abundant well differentiated mucous cells. High grade with solid and predominant squamous and intermediate cells. Immunohistochemically positive for cytokeratin. There can be variable staining for EMA, CEA, and S-100. p63 immunoreactivity can be demonstrated in the intermediate, squamous and clear cells, Bilal H et al (2003). Mucoepidermoid carcinoma often expresses CK7, Nikitakis N G et al (2004). It can be differentiated from Necrotizing sialometaplasia by presence of normal lobules of minor salivary gland, necrosis, dense inflammatory infiltrate, lack of cytologic atypia in the latter. Likewise Adenosquamous carcinoma and Squamous cell carcinoma have true squamous differentiation with intercellular bridges or keratinization with surface and squamous dysplasia or carcinoma in situ.

Cure is possible, especially for low-and intermediate-grade tumours. High profiferative index, vascular invasion, involved margins, and aneuploidy are also associated with a poor prognosis, Pires F R et al (2004); Handra Luca A et al (2005). Treatment is wide local excision.

Polymorphous low-grade adenocarcinoma (PLGA)

It is characterized by infiltrative growth, morphologic diversity, and cytologic uniformity. Other designations include lobular carcinoma, terminal duct carcinoma and low-grade papillary adenocarcinoma. PLGA occurs almost exclusively in the minor salivary glands. Only rarely does it occur in the major glands, in that setting most often being the malignant component in carcinoma *ex* pleomorphic adenoma, Nagao T et al (2004). The commonest site of occurrence is the palate (60-70), followed by buccal mucosa (16%), upper lip (12%), retromolar area, base of tongue, Ellis G L et al (1996); Castle J T et al (1999). The peak age of presentation is in the fifth and sixth decades, but children can also be affected, Tsang Y W et al (1991) and there is a female predominance.

Clinically the tumor presents as an asymptomatic mass with or without ulceration. Grossly circumscribed, nonencapsulated, pale yellow or tan mass of 1 to 3 cm. Microscopically solid nests, lobules, cribriform gland like structure or duct- like arrangements seen. Common feature is concentric whorling of cellular nests in a single file arrangement in a pattern “the eye of the storm”. The stromal hyalinization is characteristic and tumor cells are quite regular with moderate ecosinophilic cytoplasm and characteristic round to oval nuclei with open chromatin. There is little mitotic activity and no necrosis and at the periphery infiltrative growth and perineural invasion are common, Perez-Ordonez B et al (1998).

A relatively diagnostic feature in PLGA is the targetoid pattern formed by concentrically arranged cords and narrow tubules of cells,

reminiscent of sclerosing adenosis of the breast. A slate gray-blue stroma is said to be characteristic, Thompson LD (2004). Dedifferentiated PLGA can rarely occur many years after the initial diagnosis or at presentation. Such lesions often resemble salivary duct carcinoma, Simpson RH et al (2002), with predominantly solid and cystic growth, high nuclear grade, and obvious tumor necrosis.

The tumor cells show immunoreactivity for cytokeratin, EMA, and S-100 protein. A proportion of the tumor cells can express p63 in a haphazard distribution, Bilal H et al (2003). PLGA should be differentiated from Pleomorphic adenoma and Adenoid Cystic carcinoma. In Pleomorphic adenoma no infiltrative growth pattern or perineural invasion is seen. There is positive staining for Gilial fibrillary acidic protein (GFAP) in a mesenchymal-like cell population adjacent to epithelial nests. Adenoid Cystic carcinoma have basaloid cells with dark chromatin and little cytoplasm and the proliferative index is higher, Skalova A et al (1997).

PLGA is a low-grade neoplasm, with more than 95% of patients being alive after a mean follow-up of 10 years, Castle JT (1999). Local recurrence and regional metastasis rates are 9-17% and 9-15% respectively, which may occur up to 14 years after initial treatment (mean, 7 years), Castle JT (1999); Evans HL et al (2000). Tumors with a predominant papillary configuration have been reported to carry a higher

incidence of cervical lymph node metastasis, Evans HL et al (2000). Treatment is conservative resection.

Acinic cell carcinoma

It is a neoplasm demonstrating at least focal differentiation towards serous acinar cells. This neoplasm does not show myoepithelial participation. It contributes 1-3% of tumors and occur in pediatric to geriatric age from second to seventh decade of life. It is a second most common childhood malignancy. The most frequent sites of occurrence are the parotid gland (84%) and submandibular gland (4%), followed by the buccal mucosa, upper lip, and palate, Ellis GL et al (1996). It is the commonest malignant tumor that may present bilaterally (3%), Gnepp DR et al (1989). A slight female predominance is observed, and the mean age at presentation is 44 years. Acinic cell carcinoma has also been reported in antronasal mucosa, larynx, mandible, breast, lung, Lee HY et al (2003) and pancreas, Ohike N et al (2004).

Acinic cell carcinoma typically presents as a slow-growing mass with or without pain. Facial nerve palsy is uncommon (5-10%), Colmenero C et al (1991); Ellis GL et al (1983). This indolent tumor pursues a protracted clinical course, Ellis GL et al (1983). In a study of 65 patients with long follow-up of up to 45 years, 44% of patients had local recurrence, 19% had metastasis and 25% died of disease, Lewis J et al (1991). Grossly there is a single, circumscribed solid mass which undergoes cystic degeneration. Microscopically it is highly variable that

is solid, lobular, microcystic, papillary- cystic or follicular. Acinic cell look like salivary acinar cell with abundant, granular, basophilic cytoplasm and a small, round, eccentrically placed nucleus.

PAS stain highlight the cytoplasmic zymogen granules resistant to diastase digestion and other cell types can also present are eosinophilic, clear, and vacuolated cells. There is dense lymphoid infiltrate (not in periphery of tumor). The nuclei are lined up in characteristic "regimented" rows. The finding of cytoplasmic vacuoles of variable sizes is highly characteristic of this tumor. Dedifferentiated acinic cell carcinoma is associated with rapid tumor growth, significant pain, facial nerve palsy, bulky tumor, and an extremely poor prognosis, Timon CI et al (2001).

Most tumor cells exhibit immunohistochemical evidence of differentiation towards acinar cells and ductal cells, such as positivity for cytokeratin (especially low-molecular-weight cytokeratin), CEA. Differential Diagnosis it shoud be differentiated from Oncocytic carcinoma and Clear cell carcinoma which are eosinophilic and have clear cell type. The papillary variant of acinic cell carcinoma must be differentiated from Cystadenocarcinoma.

Overall survival probabilities are 90% at 5 years, 83% at 10 years, and 67% at 20 years. Therefore lifelong follow-up is imperative, even after apparently complete excision, Lewis J et al (1991). Acinic cell

carcinomas arising from the minor glands appear to be associated with a better prognosis, Ellis GL et al (1996).

Frequent mitosis or high proliferative index, focal necrosis, neural invasion, gross invasion, desmoplasia, atypia and depletion of stromal lymphocytes have been associated with more frequent recurrences and metastasis, Ellis GL et al (1996); Hamper K et al (1990); Lewis J et al (1991). Dense lymphoid stroma with well-developed germinal centers and showing a microcystic growth pattern throughout have a particularly favorable prognosis (no recurrence or metastasis on follow-up of 19 months to 14 years), Michal M et al (1997). Treatment of choice is complete surgical excision, supplemented by postoperative radiotherapy if the resection margin is involved.

Adenoid Cystic Carcinoma

It is an invasive neoplasm composed predominantly of basaloid cells with myoepithelial/basal cell differentiation, accompanied by interspersed ductal structures. It is characterized by cribriform, and /or solid patterns of growth and a myxohyaline stroma, Perzin KH et al (1978). Adenoid cystic carcinoma most commonly presents in the fourth to sixth decades, with a slight female predominance. The parotid gland, submandibular gland and palate are most commonly involved. This tumor has also been reported in lacrimal glands, auditory canal, upper respiratory tract, lung, digestive track, skin, breast, prostate and lower female genital tract, Lassaletta L et al (2003).

It is a slow growing swelling and large tumors often cause fixation to skin or deeper tissues. There may also be tenderness, pain and facial nerve palsy due to the marked propensity of the tumor for neural invasion, Friedrich et al (2003). Palatal tumors often ulcerate and bone invasion may occur without radiographic changes as the tumor infiltrate through the marrow spaces. The tumor has often invaded well beyond the clinically apparent borders, Matsuba HM et al (1986); Nacimento AG et al (1986). It is a most recoganizable tumor and comprises 10% of salivary gland malignancies, the peak incidence occur between 40 to 60 years of age. It is slow growing relentlessly progressive and perineural invasion is extremely common, so cranial nerve involvement, facial nerve palsy may be symptoms. Grossly solid, light tan, firm and well circumscribed.

Microscopically, there are three type of growth patterns are seen cribriform, tubular, soild and mixed. Infiltrative growth is usually obvious on histologic examination, and perineural invasion is very common. The three characteristic growth patterns are present in variable combinations in an individual case. In Tubular pattern double cell lined ducts are present. Solid type has only lobules of tumor cells without defined architecture. Solid growth pattern is rarely present in a pure form, and if so, may be extremely difficult to recognize, Batsakis J et al (1999). Cribriform type is classic and most easily recognisable nests of cells arranged around gland – like spaces filled with PAS positive, granular basophilic material. Cells are basaloid with little cytoplasm and round to

oval nuclei dark and hyperchromatic without nucleoli, quite regular with little mitotic activity (except solid type).

In contrast to pleomorphic adenoma, there is no “melting” of the basaloid cells into the stroma. The stroma is fibrous with variable amounts of myxohyaline material rather than desmoplastic, and cartilage is not formed.Dedifferentiation of adenoid cystic carcinoma is associated with bulky disease, frequent local recurrence and metastasis, and rapidly fatal outcome, Nagao T et al (2003).

Diagnosis and immunohistochemical staining confirms the predominant myoepithelial differentiation of the basaloid cells. These cells express cytokeratin, vimentin, S-100 protein (usually patchy staining), actin (variably), calponin, and p63, Emanuel P et al (2005) whereas the interspersed ductal epithelial cells express cytokeratin strongly, CEA and EMA.

Low grade (tubular) tumor should be differentiated from Polymorphous low-grade adenocarcinoma, Epithelial-myoepithelial carcinoma and basal cell adenocarcinoma. All these three have no basaloid and hyperchromatic nuclei. Solid type high grade neuroendocrine carcinoma should be differentiated from Basaloid Squamous cell carcinoma which is bland appearing. Tumor showing tubular and cribriform patterns represent lower-grade growths, Batsakis JG et al (1999); Batsakis JG et al (1990). The solid pattern is associated

with large tumor size, earlier and more frequent recurrence, higher incidence of metastasis and earlier fatal outcome, Hamper K et al (1990).

It is found that carcinomas with significant solid areas (>30% of tumor area) have cumulative 5-year and 15-year survival rates of only 14% and 5% respectively, compared with 92% and 39% for tumors without a significant solid component, Szanto PA et al (1984). Advanced clinical stage, location in a minor gland, large tumor size (>2-4cm), bone invasion, positive excision margins, non-diploid DNA content, high S-phase fraction, and high Ki67 index have been reported to be poor prognostic factors, Hamper K et al (1990); Kokemueller H et al (2004).

Long- term prognosis is poor. The 5-year survival is about 60-75%, but the 10-year survival drops dismally to 30-54%, Kokemuellur H et al (2004). The majority of affected patients (80-95%) eventually die of the disease after a protracted clinical course characterized by multiple local recurrences and metastasis, Hamper K et al (1990). Distant metastasis (most commonly lung, bone, and soft tissue) is more common than regional lymph node metastasis, and often occurs 5-10 years after initial treatment, Rapidis AD et al (2005). Radical excision is the treatment of choice and benefit of radio therapy remains unproven, Friedrich RE et al (2003); Kokemueller H et al (2004).

Malignent mixed tumor

(i)True salivary gland malignant mixed tumor (carcinosarcoma)

It composed of both carcinomatous and sarcomatous components and 2/3 tumour arise from parotid gland, 15% submandibular gland and 15% from palate. It is a very aggressive tumor and 1/3 die within 30 month of time. Occurence of this tumour is very rare and the mean age at presentation is 62 years with no sex predilection. The tumor most frequently affects the major salivary glands. In one-third of cases, there is clinical or histologic evidence of coexisting pleomorphic adenoma, Kwon MY et al (2001).

Grossly the tumour is firm, tan-white mass with hemorrhage, necrosis occasionally with grittiness or calcification. Microscopically there is intimate mixture of two components that is malignant epithelial and mesenchymal elements. The epithelial component is most often a squamous cell carcinoma or adenocarcinoma and the most common malignant mesenchymal component is chondro sarcoma, followed by fibrosarcoma, leiomyosarcoma, osteosarcoma, liposarcoma, and rhabdomyosarcoma, Kwon MY et al (2001); Gnepp DR (1993). It is an aggressive tumor with a mean survival of only 29.3 months, Gnepp DR (1993). Treatment is wide local excision with radiotherapy.

(ii) Carcinoma ex pleomorphic adenoma

Carcinoma ex pleomorphic adenoma represents malignant transformation of a pre-existing pleomorphic adenoma usually in the setting of long-standing pleomorphic adenoma or in a tumor with multiple recurrences. The incidence ranges from 1.9% to 23.3% (mean

6.2%) according to different series, Auclair PL et al (1996). It occures mostly in parotid gland and during sixth to seventh decade of life. Long standing mass undergo rapid growth over a period of several months is a classic history of this tumour. The risk increases with the duration of the tumor, with an incidence of 1.6% for tumors presenting for less than 5 years, increasing to 9.5% for tumors presenting for more than 15 years, Eneroth CM et al (1974).

The tumor is usually larger than its benign counterpart. Grossly the tumour may be up to 25cm and carcinomatous component is infiltrative, hard, white to gray mass with hemorrhage and necrosis. Malignant transformation is heralded by rapid growth after a long period of a minimally perceptible increase in size. Signs of malignancy also include fixation to surrounding tissues, ulceration, facial nerve palsy, and regional lymphadenopathy. The mean age at presentation is 61 years, about one decade older than that of pleomorphic adenoma, Lewis JE et al (2001); Ellis GL et al (1996).

Histologically, the malignant component is characterized by widespread significant cellular pleomorphism, a high mitotic count, atypical mitotic figures, coagulative necrosis and the presence of an expansile or infiltrative nodule within the parent adenoma. In most cases, the malignant component dominates the tumor, and is most frequently a high-grade carcinoma (85% of cases) such as adenocarcinoma NOS or salivary duct carcinoma but sometimes maybe

adenosquamous carcinoma, undifferentiated carcinoma, or sarcomatoid carcinoma. Low-grade carcinomas such as PLGA, adenoid cystic carcinoma, mucoepidermoid carcinoma, epithelial myoepithelial carcinoma and myoepithelial carcinoma can also occur infrequently, Lewis JE et al (2001); Ellis GL et al (1996).

The most important prognostic factor is the extent of extra capsular invasion. Carcinoma in situ and intracapsular carcinoma have no metastatic potential, Lewis JE et al (2001). In several large series, excellent prognosis has been found in tumors with extracapsular invasion less than 8mm, Tortoledo ME et al (1984) 5mm, Lewis JE et al (2001) beyond the capsule respectively. Poor outcome has been found to be associated with: (1) high histologic grade of malignant component (5-year survival 30% versus 96% for low histologic grade); (2) high pathologic stage; and (3) proportion of carcinoma more than 50% of the tumor, Lewis JE et al (2001); Tortoledo ME et al (1984). Most patients develop recurrence and metastasis, and the overall 5-year survival is only 30%, Lewis JE et al (2001). Treatment is wide resection and radiation for widely invasive tumors. If cervical lymphnode metastasis is present lymph node dissection should also be done.

(iii) Metastasizing mixed tumor

Metastasizing pleomorphic adenoma is a rare complication of pleomorphic adenoma. Generally, metastasis occur after a relatively long period. Rarely, the metastatic tumor may represent the initial

manifestation of an occult plemorphic adenoma in the salivary gland, Czader M et al (2000).

The disease apparently pursues a more rapidly aggressive course in immunocompromised hosts, Sampson BA et al (1998). Malignant transformation of metastatic pleomorphic adenoma has also been reported, Fujimura M et al (1997). Vascular permeation secondary to mechanical implantation has been postulated as a probable mechanism for the development of metastasis, Hoorweg JJ et al (1998). Treatment is local excision of both the primary and metastatic tumors. Recur at primary site and the mortality rate is 40%.

Salivary duct carcinoma

Salivary duct carcinoma is an aggressive malignant tumor morphologically reminiscent of ductal carcinoma of the breast. It can occur de novo or as the malignant component in carcinoma ex pleomorphic adenoma, Delgado R et al (1993); Jaehne M et al (2005). Salivary duct carcinoma most frequently affects the elderly (peak incidence in the sixth and seventh decades), with a male to female ration of 3-6:1. The parotid gland accounts for 80% of cases and the rest arise in the submandibular gland, and rarely, minor glands of the oral cavity. The patients commonly present with a rapidly enlarging parotid mass associated with facial nerve palsy (42%), pain (23%) and cervical lymphadenopathy (35%), Lewis JE et al (1996).

Grossly there is poorly circumscribed, predominantly solid, and tan-colored. There are often foci of necrosis. Gross extension of tumor beyond the salivary gland is noted in about 70% of cases, Lewis JE et al (1996). Microscopically cribriform pattern similar to breast ductal carcinoma with comedo-type necrosis and invasive component consist of large cells with abundant eosinophilic cytoplasm and large, round nuclei with vesicular chromatin and prominent nucleoli. Marked tissue infiltration with stromal desmoplasia and brisk mitotic activity and vascular and perineural invasion are common, Barnes L et al (1994).

Diagnosis by luminal epithelial nature of the tumor cells, with diffuse strong staining for cytokeratin, EMA, and CEA. Almost all cases express androgen receptor, which is a characteristic, although not specific, feature of this salivary gland carcinoma, Nasser SM et al (2003). It should be differentiated from metastatic breast carcinoma which is positives for estrogen/ progesterone receptor, and negative for androgen receptor. Also differentiated from Mucoepidermoid carcinoma which have mixture of cell types such as epidermoid cells and goblet cells and intraductal carcinoma which is primary salivary duct carcinoma than metastasis. Oncocytic carcinoma is characterized by large tumor cells with granular eosinophilic cytoplasm filled with mitochondria. Both oncocytic carcinoma and cystadenocarcinoma lack the comedo necrosis and intraductal-like pattern typically seen in salivary duct carcinoma.

This is one of the most aggressive salivary gland carcinomas. The tumor mortality can be as high as 77% at a mean follow up of 3 years, Lewis JE et al (1996). Local recurrence occurs in 35-66% of patients, lymph node metastasis in 66% and distant metastasis in 50-70%, Lewis JE et al (1996); Guzzo M et al (1997). The most frequent sites of distant metastasis are the lung, bone, and brain and with 65% of mortality. Treatment is wide local excision with neck dissection and postoperative radiotherapy.

Epithelial – Myoepithelial carcinoma

Composed of ductal structures lined by a single layer of ductal cells which are surrounded by a single or multiple layers of clear myoepithelial cells. The counterpart in the breast is adenomyoepithelioma, Seifert G (1998). It is a low grade tumor and accounts for 0.5 to 1%. The peak incidence is in the sixth and seventh decades, with a slight female predominance. Approximately 60% of cases occur within the parotid gland, while submandibular gland and intraoral minor salivary gland are responsible for the rest. Most patients present with an asymptomatic mass, and a minority of patients have pain and facial weakness. The tumor has also been reported to occur in lacrimal gland, lung, bronchus, trachea, nasal cavity, nasopharynx and liver, Ru K et al (2004); Doganay L et al (2003).

Grossly the tumour is firm and well-demarcated with 2-cm diameter. It will be partially encapsulated, with invasion into adjacent

parenchyma. Microscopically classic morphology is ductal structures lined by eosinophilic cells with a prominent supporting layer of clear myoepithelial cells, myoepithelium present as large sheets of cells with only focal ductal differentiation. The stroma between tumor nests is eosinophilic and hyalinized, individual tumor cells are bland with minimal mitotic activity. The prototypic bicellular architecture consists of a tubular structure lined by ductal cells, surrounded by one or several layers of clear cells, which are further enveloped on the outside by a well-defined basement membrane. The tubular luminal cells are cubodial, with round, bland- looking nuclei and a moderate amount of pink cytoplasm, reminiscent of intercalated duct cells. Rarely, there can be squamous differentiation. The clear cells are polygonal, considerably larger in size and have abundant water-clear cytoplasm. The cytoplasmic clearing is due to accumulation of glycogen. These cells exhibit a myoepithelial immunophenotype and ultrastructural features.

Immunohistochemically, the duct- lining cells are positive for cytokeratins and myoepithelial cells are positive for calponin, smooth muscle actin and p^{63}, Alos L et al (1999). It should be differentiated from Pleomorphic adenoma myoepithelioma/Myoepithelial carcinoma which do not have myoepithelial differentiation. Also differentiated from tubular variant (Grade I) adenoid cystic carcinoma which have no clear cells, if present very focal. There is cribriform structures and light basophilic mucosubtance in microcystic spaces.

Epithelial-myoepithelial carcinoma is a relatively low-grade malignancy. Recurrence is reported in 30-40% of cases, which may occur as long as 28 years after initial surgery. Regional lymph node metastasis occurs in 10-20% of cases, but distant metastasis (lung, kidney and brain) is uncommon (90%). Tumor-associated mortality is low (0-90%), Luna MA et al (1987). Also reported that tumors with more than 20% of cells showing nuclear atypia are associated with a poorer prognosis, Fonseca I et al (1993). Treatment is wide local excision with or without radiotherapy.

Squamous cell carcinoma

This tumor mainly affects males, with a mean age of 64 years, Prior radiation therapy for acne, benign and malignant tumors, enlarged thymus, thyroid gland and tonsils have been implicated as predisposing factors in some cases, Ellis GL et al (1996). It is a aggressive tumour, rarely primary and is metastasis to intraparotid lympnode from primary skin cancer of head and neck (scalp, ear and face). It occurs during sixth to eighth decade of life and seen in 80% parotid, 20% in submandibular gland.

Grossly firm, white, infiltrative and nonencapsulated mass. Histologically it is usually a moderately to well – differentiated squamous cell carcinoma consisting of sheets and islands of squamous cells with readily identifiable keratin formation and intercellular bridges. There is

prominent desmoplasia and Perineural invasion into periglandular soft tissue is frequently present.

It should be differentiated from metastatic squamous cell carcinoma and also from high grade mucoepidermoid carcinoma which is largely squamoid appearance but lack keratinization, more heterogenous cell population and always demonstrates mucous cells. Ulceration, fixation, advanced patient age, advanced tumor stage and facial nerver palsy are unfavorable prognostic factors, Gaughan R et al (1992). The 5-year survival rate is only around 30%. Treatment is radical surgery, neck dissection and radiotherapy. Squamous cell carcinoma tends to invade and spread rapidly. Since cervical lymph node metastasis is common, routine radical neck dissection may be advisable.

Adenocarcinoma

It is a rare, but aggressive tumour. It occurs above 40 years of age and mostly parotid and minor salivary gland are affected. Clinically 25% complain of pain or facial weakness. Grossly firm mass with irregular border and infiltration into surrounding tissue. It is a solid tumour without cystic spaces. Formation of glandular structures are divided in to Grade I to IV. Grade I is well formed ductal structures and II is more solid growth pattern with few glandular characteristics. Treatment is complete local excision and metastasis is common. The recurrence rate is 51%.

Clear cell carcinoma

Also called as glycogen rich carcinoma. It is a rare tumour and occur in palate & parotid gland. It is seen between sixth to eighth decade of life. Microscopically uniform round polygonal cells with peripherally displaced dark nuclei and clear cytoplasm was seen. Tumor cell grow in nests or cords separated by fibrous stroma or solid sheets of cells. Local infiltrative growth is characteristic of this tumour. Treatment is complete local excision.

Pediatric tumors

These are uncommon tumours. There are two congenital tumors reported.

(i) Sialoblastoma

It is rare, aggressive tumor and occur at embryonic stage. It develop from blastomatous cells and seen in perinatal to neonatal period and mostly in parotid gland. Grossly, it is lobulated and partially circumscribed. Microscopically nests or nodules of basaloid cells are seen with scanty cytoplasm, round to oval nuclei, and fine chromatin with small nucleoli. Treatment is complete surgical excision with a rim of normal tissue.

(ii) Salivary anlage tumor (Congenital pleomorphic adenoma)

It occurs in male neonates in first 2 weeks of age. The tumour mass attached by thin stalk to posterior nasal mucosa or nasopharynx. Grossly firm & tan yellow with smooth surface. Microscopically nonkeratinizing squamous epithelium, with deep stroma composed of bland spindled cells

and intervening squamous is lands suggests a hamartoma. Treatment is simple excision.

Metastasis to the salivary gland

Metastasis to the salivary gland from intra or periglandular was lymph nodes are common. For parotid gland usually head and neck primary tumor. Skin tumors such as squamous cell carinoma and melanoma accound for 80% of metastasis. 85% of submandibular gland metastasis are from non head and neck tumors, from infraclavicular areas scommonly breast, kidney and lung (small cell carcinoma of the lung).

MATERIALS AND METHODS

This study included salivary gland biopsy specimens submitted for histopathological study to the Department of Pathology, Tirunelveli Medical College from 2006 to 2010. The demographic data regarding age, gender, location of lesion, duration, associated symptoms were recorded in a proforma.

Detailed gross examination was done and the findings were recorded.

4 micron sections were cut and stained with routine haematoxylin and eosin stains. Based on the histopathology, the lesions were categorized into neoplastic and non neoplastic lesions. The neoplastic lesions were further divided into benign and malignant types. The malignant tumor were further typed histologically into various categories. Special stains like Periodic acid Schiff (PAS), Alcian blue and Phosphotungstic acid stain also done.

Haematoxylin and Eosin staining

1. Xylene, three changes….. 2minutes each
2. Absolute alcohol….. 10 dips
3. 90% alcohol, 80% alcohol,
   and 70% alcohol…… 10 dips each
4. Tap water…. rinse until water runs off evenly
5. Haematoxylin,….. 15 minutes
6. Tap water, two changes …… 10 dips each

7. Lithium carbonate, 0.5% …. Until blue
8. Tap water, two changes….. 10 dips each
9. Eosin ……. 10 to 20 dips
10. 70% alcohol, 80% alcohol and 90% alcohol …… 10 dips each
11. Absolute alcohol, three changes… 10 dips each
12. Xylene, three changes….. 10 dips each
13. Mount the slide in D.P.X

Periodic Acid Schiff (PAS) staining

1. Cut paraffin sections ate 4 to 5 microns thick
2. Deparaffinize and hydrate slides to distilled water.
3. Wash slides in three changes of distilled water.
4. Place the section in Periodic acid for 5 minutes.
5. Water wash for 1 minute.
6. Place sections in Schiff reagent for 15 minutes.
7. Wash for 1 minute in each of two jars of 0.55% potassium Metabisulfite to remove excess stain.
8. Wash in running tap water for 10 minutes to develop full color.
9. Counterstain ½ minute in Harris' hematoxylin with acetic acid (2ml acetic acid/48 ml haematoxylin)
10. Wash sections well to blue the haematoxylin.
11. Dehydrate with 95% and absolute alcohol, clear with Xylene and mount the section.

Alcian Blue Staining

1. Cut paraffin sections at 4 to 5 micron thickness
2. Deparaffinize and hydrate sections to distilled water.
3. Place slides in 3% acetic acid solution for 3 minutes.
4. Place slides in alcian blue solution for 30 minutes.
5. Wash slides in running tap water for 10 minutes.
6. Rinse in distilled water.
7. Counterstain in nuclear fast red solution for 5 minutes.
8. Wash in running tap water for at least 1 minute.
9. Dehydrate in two changes each of 95% alcohol and absolute alcohol and clear in Xylene.
10. Mounting.

Phosphotungstic acid Staining

1. Deparaffinize, hydrate through graded alcohols to water.
2. Place in acid dichromate solution for 1 minute.
3. Wash in tap water.
4. Treat with acid permanganate solution for 1 minute.
5. Wash in tap water.
6. Bleach in 1% oxalic acid.
7. Rinse in tap water.
8. Stain in Mallory's PTAH stain overnight.
9. Dehydrate through graded alcohols, clear and mount.

Special stains for various neoplasms

Neoplasm	Special Stain
Pleomorphic adenoma	Alcian blue
Acinic cell carcinoma	Periodic Acid Schiff
Mucoepidermoid carcinoma	Periodic Acid Schiff
Adenoid cystic carcinoma	Periodic Acid Schiff
Oncocytoma	Phospho tungstic acid hematoxilin

The results were analyzed, tabulated as percentage proportion and compared with the existing literature.

RESULTS

There was totally 80 salivary gland lesions from both outpatient and inpatient during the 5 year period between 2006 to 2010. The age of occurrence was from 10 years to a maximum of 80 years with mean age of 41.19 years. Of these, 32.5% in males and 67.5% in females. The distribution of lesion was 71.25% in parotid, 25% in submandibular gland, 2.5% in accessary gland and 1.25% in sublingual gland.

Out of the 80, there were 17 (21.25%) non neoplastic with mean age 38.51 and 63 (78.75%) neoplastic lesions with mean age of 41.89. Of the non neoplastic lesions 16 (94%) were sialadenitis and 1 (5.87%) was sialolith. Among neoplastic lesions 50(79.4%) was benign and 13 (20.6%) was malignant. Most common benign tumour was pleomorphic adenoma 42(84%) and most malignant tumour was mucoepidermoid carcinoma 3(23%) and acinic cell carcinoma 3(23%). The distribution of salivary gland lesion is given in graph-1 and sex distribution in Table.1

Sialadenitis seen in the age group of 15 to 56 years and 62.5% of cases occurred in 30-50 years of age. The mean age was 38 years. It involves 10(62.5%) of females and 6(37.5%) males. Out of the 16, 11 (68.75%) was seen in submandibular and 5(31.25%)was seen in parotid gland. Sialadenitis show statistical significant difference in relation to age, sex and occurrence in parotid gland. There is no significant

difference in relation to occurrence in submandibular gland. One case of sialolith was recorded in a female at the age of 48 in submandibular gland.

Salivary gland tumours recorded were 63 (78.75%) cases. It occurred between 10 to 80 years of age and 76.19% of tumours occurred at the age group of 20-60 years. Among benign tumours peak incidence of 24% was recorded in 2^{nd} and 3^{rd} decades followed by 20% in 4^{th} decade. In malignant tumours 23% occurred at 5^{th} decade followed by 15.3% in 2^{nd} to 7^{th} decades of life.

It was seen 31.75% in males and 68.25% in females with a male female ratio of 1:2.15. Among this benign was 50 (79.3%) with male female ratio of 1.5:2.65 and mean age of 40.18. Malignant was 13 (20.6%) with male female ratio of 1:5.5 and mean age of 48.46. Largest number of tumours occurred in parotid gland 52(82.5%), followed by submandibular 8 (12.7%) then accessary gland 2(3.17%) and sublingual gland 1(1.59%). Salivary gland tumour shows statistical significant difference in relation to sex, age and occurrence in salivary gland except age wise distribution of malignant salivary gland tumour. Different type of tumours recorded were given in Table-2.

The most predominant neoplasm was Pleomorphic adenoma with 42 (66.66%) out of 63 total neoplasms and with the peak occurrence in 3^{rd}

decade 10 (23.8%) followed by 2nd and 4th decade with 9 (21.4%). Male female ratio was 1:1.625. Most tumour occurred in parotid 36 (85.7%) followed by submandibular 4 (9.5%) then sublingual 1 (2.38%) and accessory gland 1 (2.38%). Pleomorphic adenoma shows statistical significant difference in relation to sex, age and salivary gland. Prevalence among male female sexes and age wise distribution are given in graph-3.

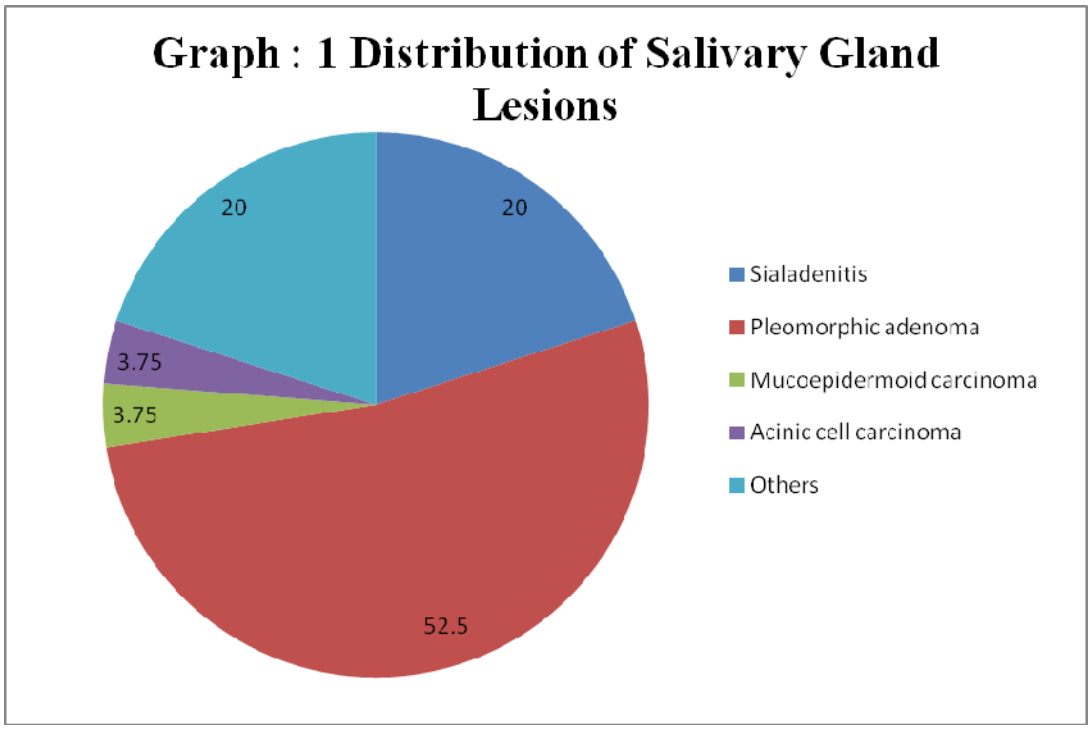
The second most common neoplasm was Mucoepidermoid carcinoma and Acinic cell carcinoma with 3 cases each (4.76%) out of 63 total neoplasms. It was seen only in parotid gland with male female ratio of 1:2. It was seen between second to seventh decade of life.

Two cases each (3.17%) recorded were Warthin's tumour, Myoepithelioma with cyst, Benign lymphoepithelial cyst, Adenocarcinoma. One cases each (1.58%) recorded were Basal cell adenoma, Monomorphic adenoma, Squamous cell carcinoma, Epithelial-Myoepithelial carcinoma, Adenoid cystic carcinoma, Adenosquamous carcinoma, Malignant oncocytoma.

Table-1

Sex wise distribution of Salivary gland lesions

S.No	Lesion	Male	Female	Total
I	Non neoplastic			
	(a) Sialadenitis	6	10	16 (20%)
	(b) Sialolithiasis	-	1	1 (1.25%)
	Total	**6**	**11**	**17(21.25%)**
II	Neoplastic			
	Benign			
	(a) Pleomorphic adenoma	16	26	42(52.5%)
	(b) Benign lymphoepithelial cyst	-	2	2(2.5%)
	(c) Myoepithelioma	1	1	2(2.5%)
	(d) Warthin's tumour	1	1	2(2.5%)
	(e) Basal cell adenoma	-	1	1(1.25%)
	(f) Monomorphic adenoma	-	1	1(1.25%)
	Malignant			
	(a) Mucoepidermoid carcinoma	1	2	3 (3.75%)
	(b) Acinic cell carcinoma	1	2	3 (3.75%)
	(c) Adenocarcinoma	-	2	2(2.5%)
	(d) Squamous cell carcinoma	-	1	1(1.25%)
	(e) Epithelial-Myoepithelial carcinoma	-	1	1(1.25%)
	(f) Adenoid cystic carcinoma	-	1	1(1.25%)
	(g) Adenosquamous carcinoma	-	1	1(1.25%)
	(h) Malignant oncocytoma	-	1	1(1.25%)
	Total	**20**	**43**	**63(78.75%)**


Graph : 1 Distribution of Salivary Gland Lesions
20
20
3.75
3.75
52.5
Sialadenitis
Pleomorphic adenoma
Mucoepidermoid carcinoma
Acinic cell carcinoma
Others

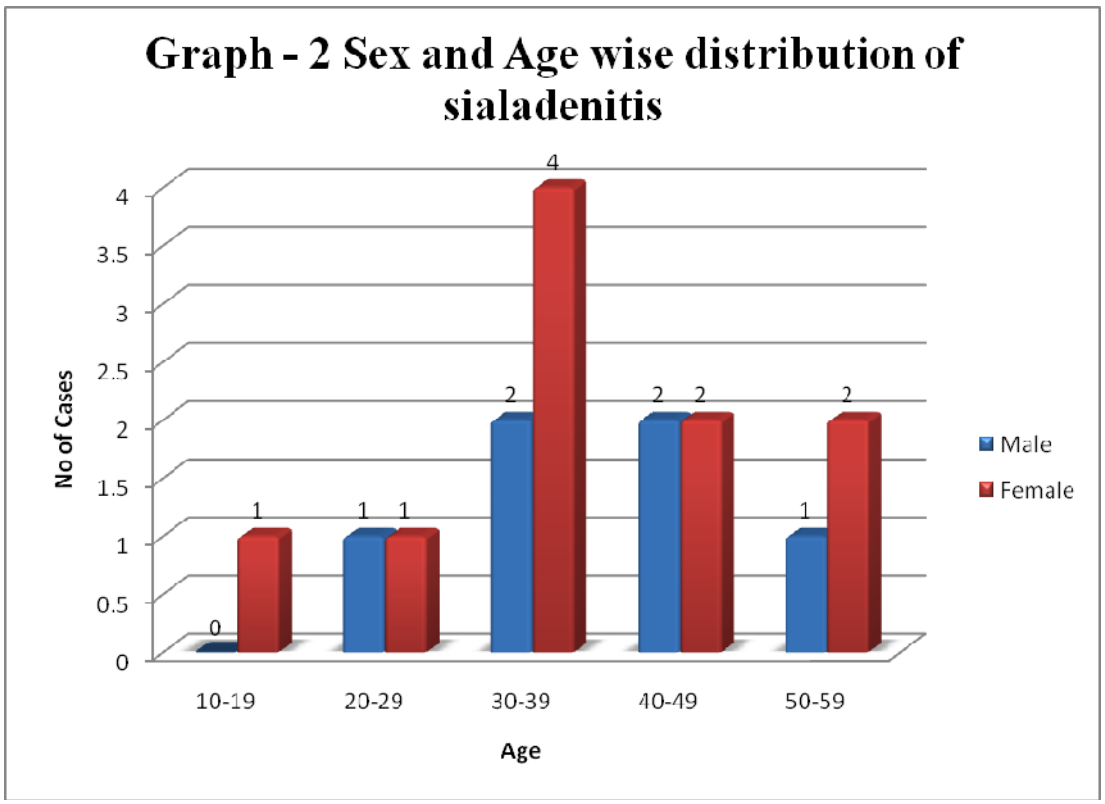
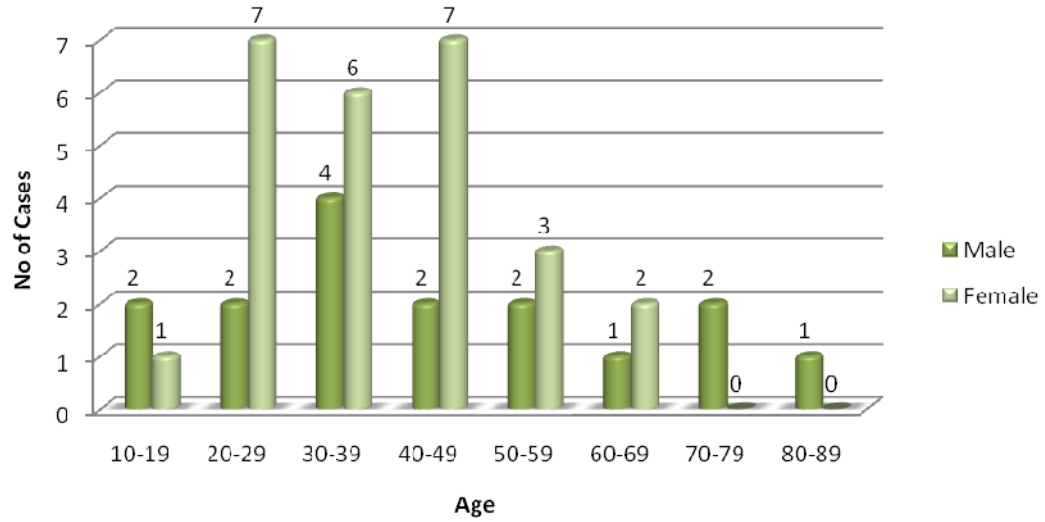

Graph - 2 Sex and Age wise distribution of sialadenitis
No of Cases
0
0.5
1
1.5
2
2.5
3
3.5
4
0
1
1
1
2
4
2
2
1
2
10-19
20-29
30-39
40-49
50-59
Age
Male
Female

Table -2

Different type of neoplasms recorded

Benign	**No. of cases**	**Percentage**
(a) Pleomorphic adenoma	42	66.6%
(b) Benign lympho epithelial cyst	2	3.17%
(c) Myoepithelioma	2	3.17%
(d) Warthin's tumour	2	3.17%
(e) Basal cell adenoma	1	1.59%
(f) Monomorphic adenoma	1	1.59%
Total	**50**	**79.37%**
Malignant		
(a) Mucoepidermoid carcinoma	3	4.76%
(b) Acinic cell carcinoma	3	4.76%
(c) Adenocarcinoma	2	3.17%
(d) Squamous cell carcinoma	1	1.59%
(e)Epithelial-Myoepithelial carcinoma	1	1.59%
(f) Adenoid cystic carcinoma	1	1.59%
(g) Adenosquamous carcinoma	1	1.59%
(h) Malignant oncocytoma	1	1.59%
Total	**13**	**20.63%**

Graph -3 Sex and Age wise distribution plemorphic adenoma



Graph - 4 Distribution of Neoplasm and Sialadenitis among salivary Glands

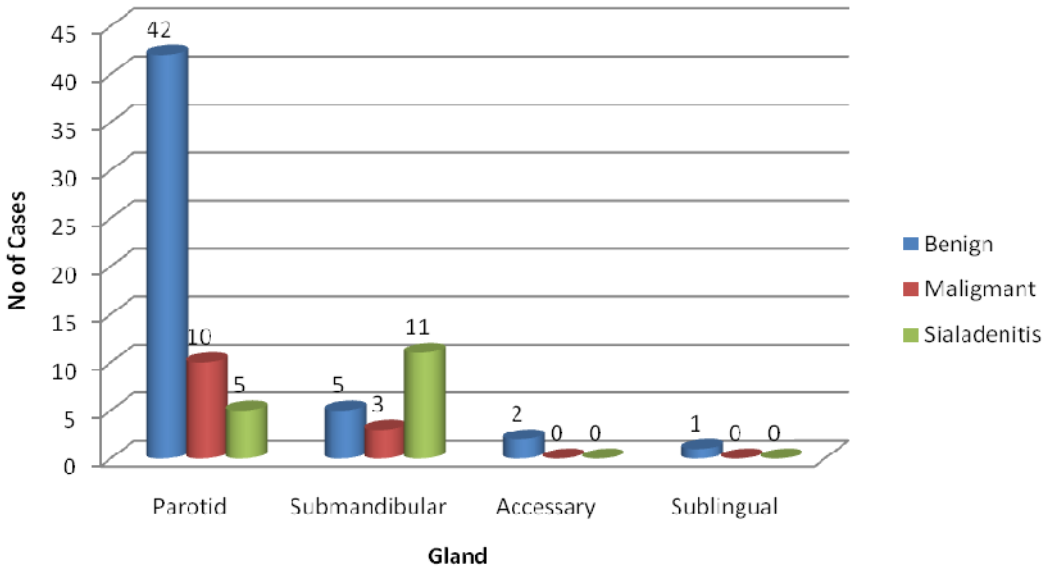
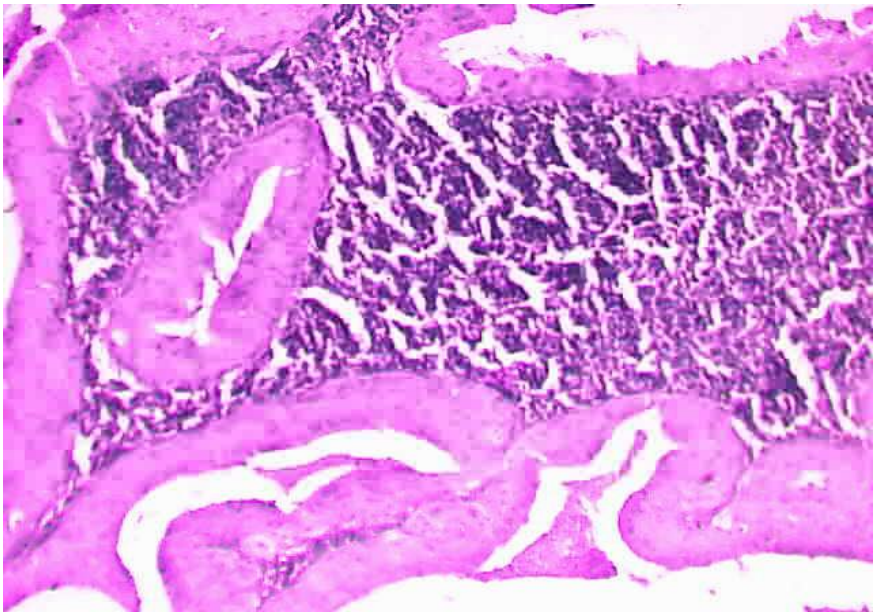


Table-3 Age wise distribution of different neoplasm types

Neoplasm	Age								
	10-19	**20-29**	**30-39**	**40-49**	**50-59**	**60-69**	**70-79**	**80-89**	**Total**
Pleomorphic adenoma	3	9	10	9	5	3	2	1	42
Benign lymphoepithelial cyst		2							2
Myoepithelioma with cyst			1	1					2
Warthin's tumour		1				1			2
Basal cell adenoma						1			1
Monomorphic adenoma			1						1
Mucoepidermoid carcinoma		1		1		1			3
Acinic cell carcinoma		1			1		1		3
Adeno carcinoma					2				2
Squamous cell carcinoma						1			1
Epithelial-Myoepithelial carcinoma				1					1
Adenoid cystic carcinoma			1						1
Adenosquamous carcinoma			1						1
Malignant oncocytoma							1		1
Total	3	14	14	12	8	7	4	1	63

Fig  1 :

Photomicrograph of Warthin's tumour [HE, x100]

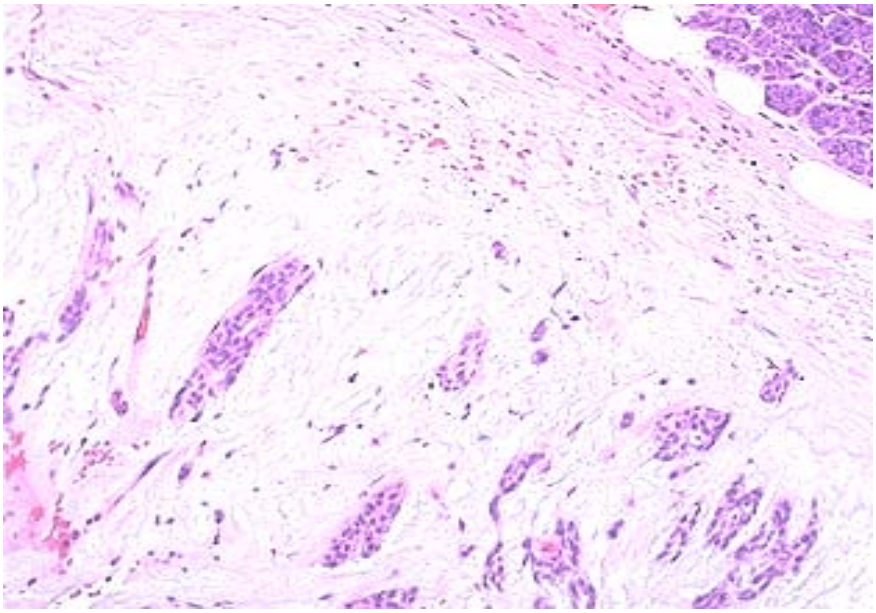


Fig 2 : Pleomorphic Adenoma Parotid { HE, x100]

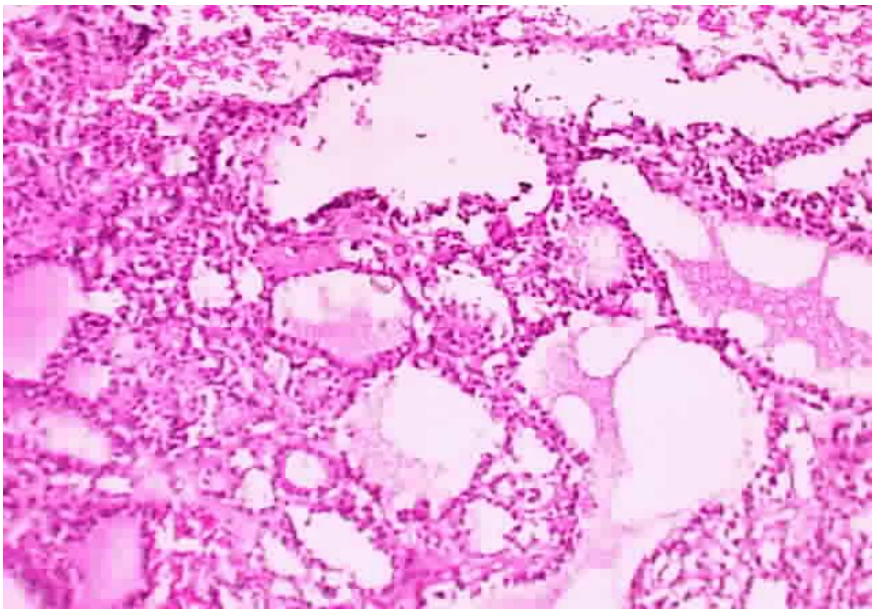


Fig 3 ; Microcystic Pattern of Basal cell adenoma [HE, x100]

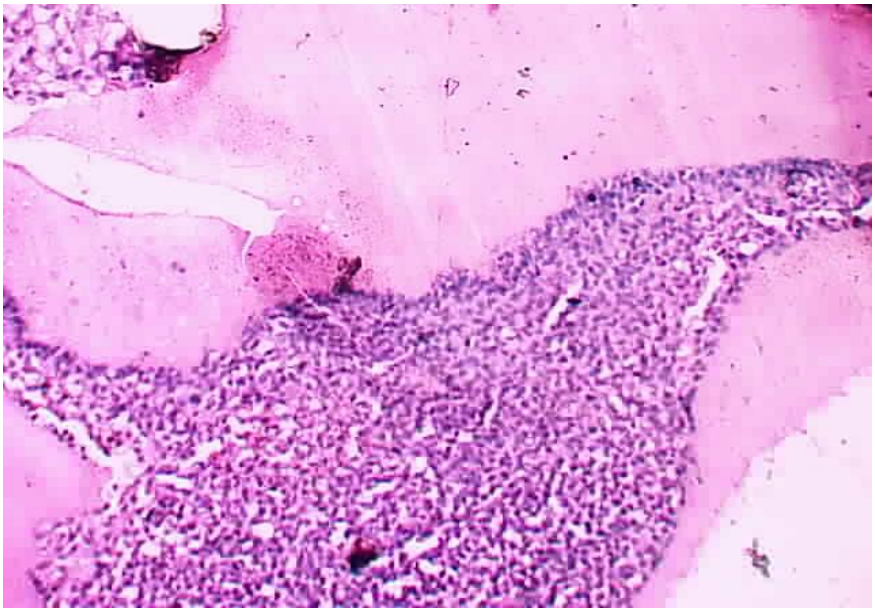


Fig 4 : Photomicrograph of Benign Lymphoepithelial Cyst [HE,x40]

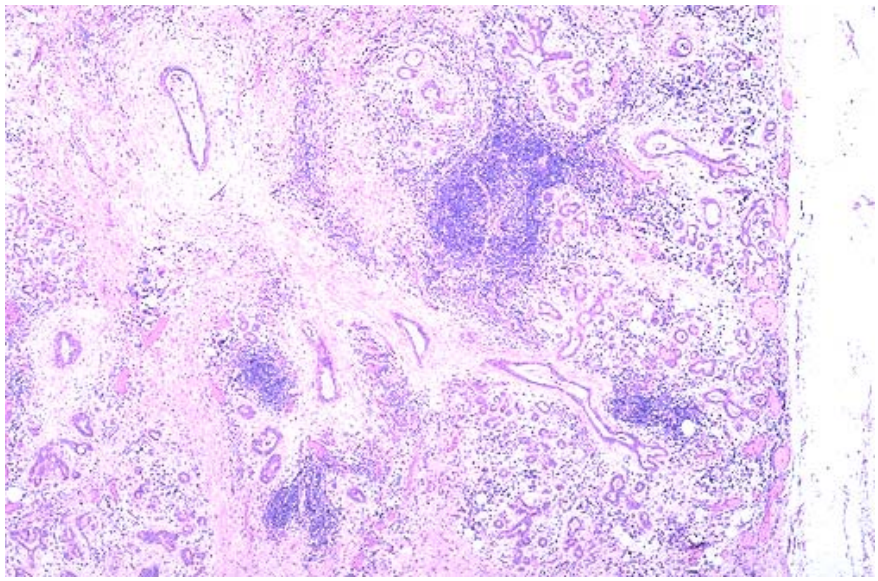


Fig 5 : Photomicrograph of Chronic Sialadenitis [HE, x100]

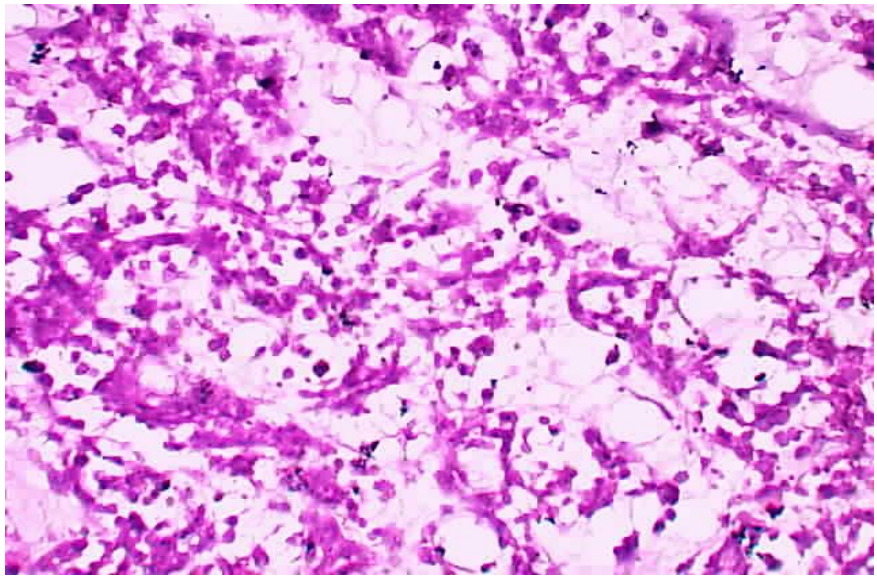


Fig 6 : Mucoepidermoid carcinoma ,mucoid areas [HE, x100]

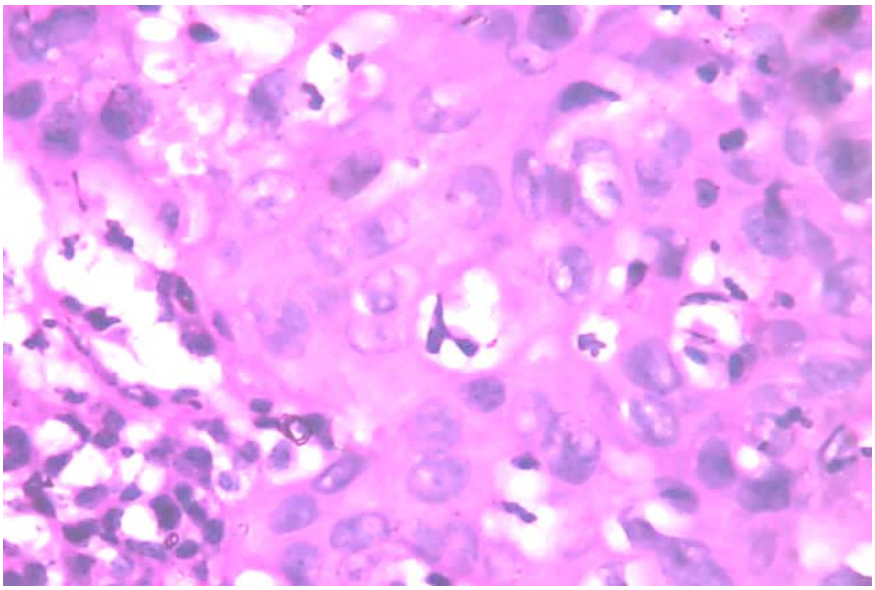


Fig 7 : Mucoepidermoid carcinoma, high grade epidermoid area [HE,x400]

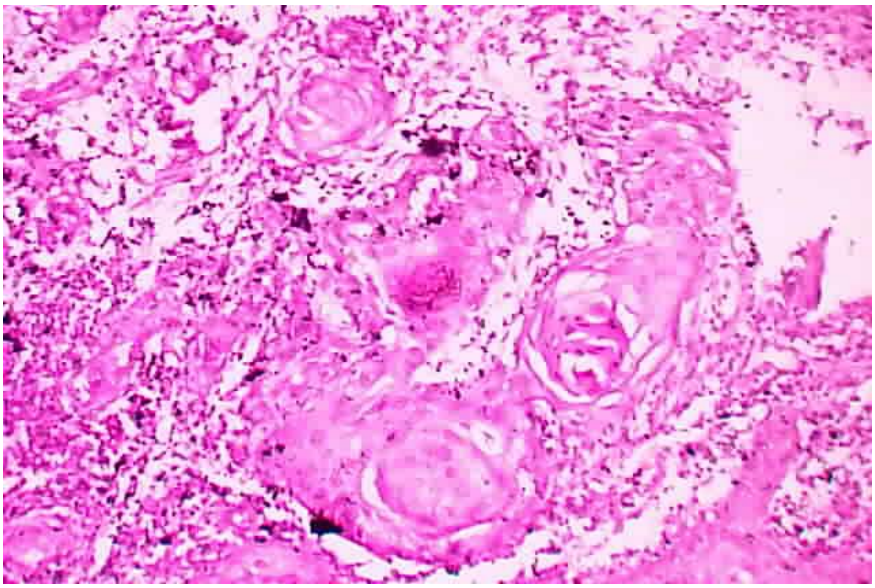


Fig 8 : Primary Keratnizing Squamous cell carcinoma [HE, x100]

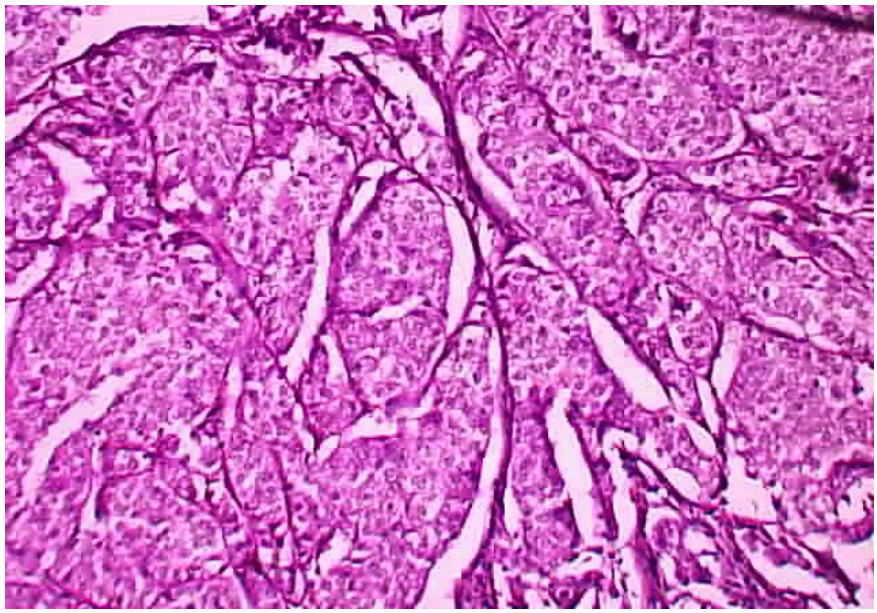


Fig 9 : Malignant Oncocytoma [HE, x100]

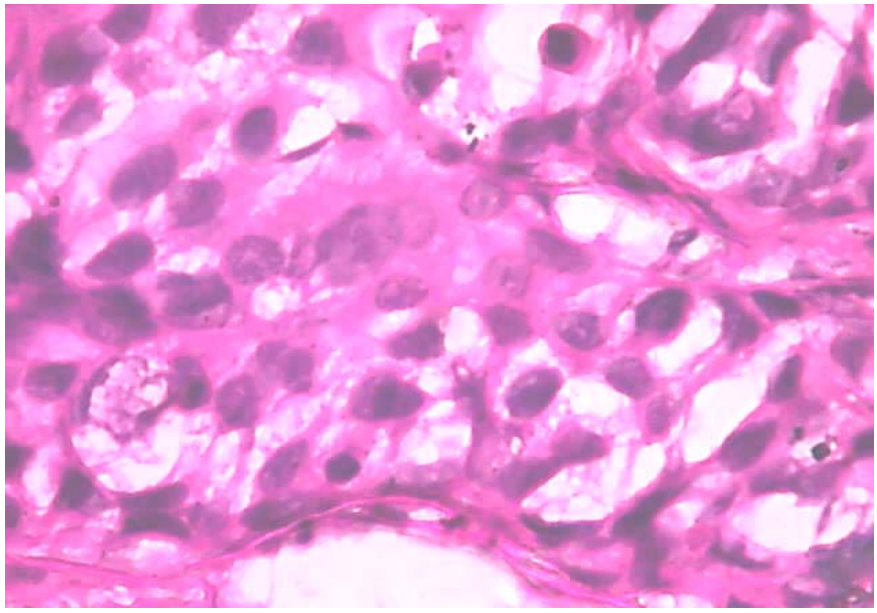


Fig 10 : Epithelial – Myoepithelial carcinoma [HE, x400]

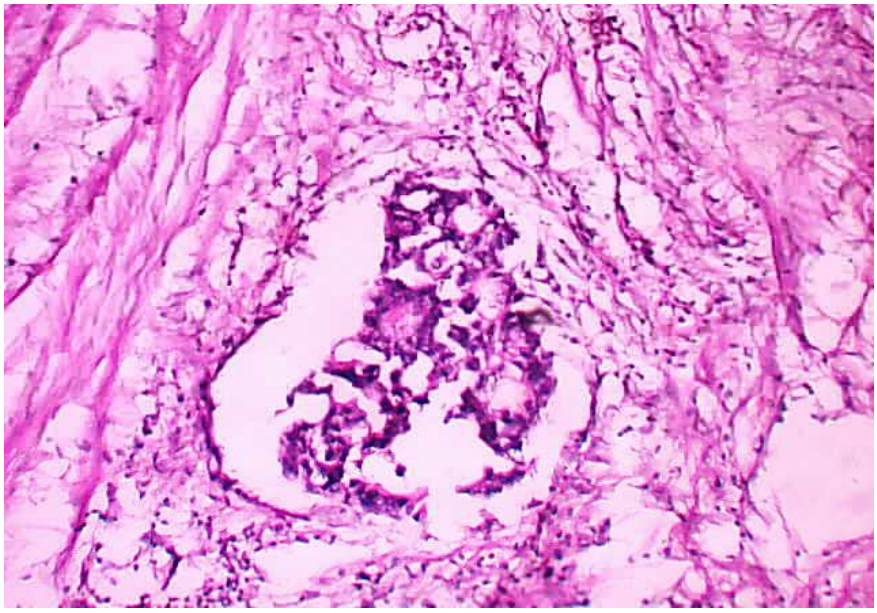


Fig 11 : Adenocarcinoma NOS type [HE, x100]

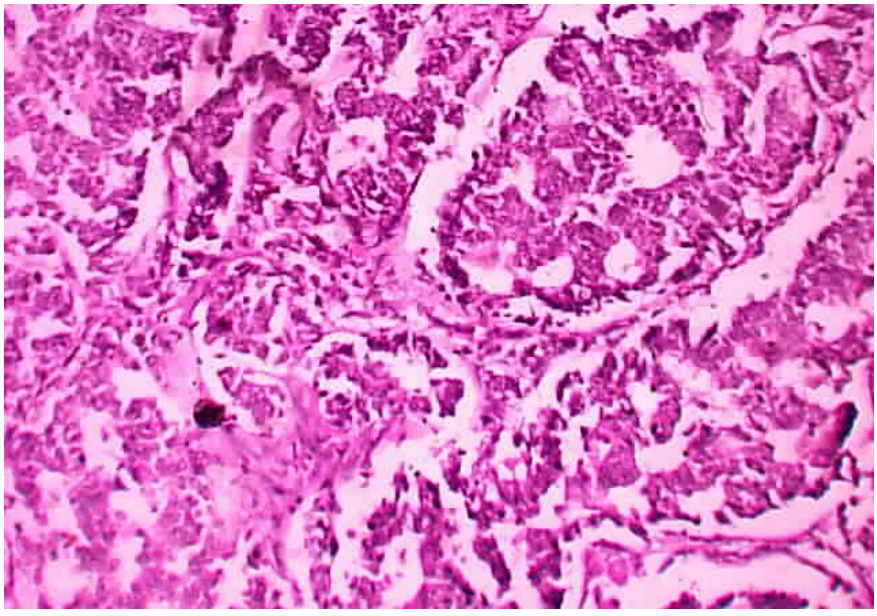


Fig 12 ; Adenoid cystic carcinoma salivary gland [HE, x100]

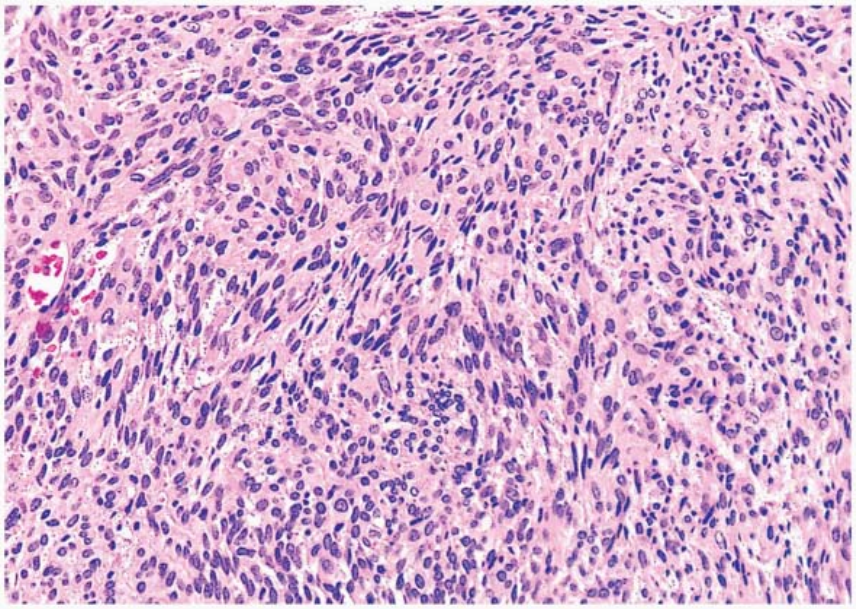


Fig 13 : Myoepithelioma Spindle cell type (HE X 100)

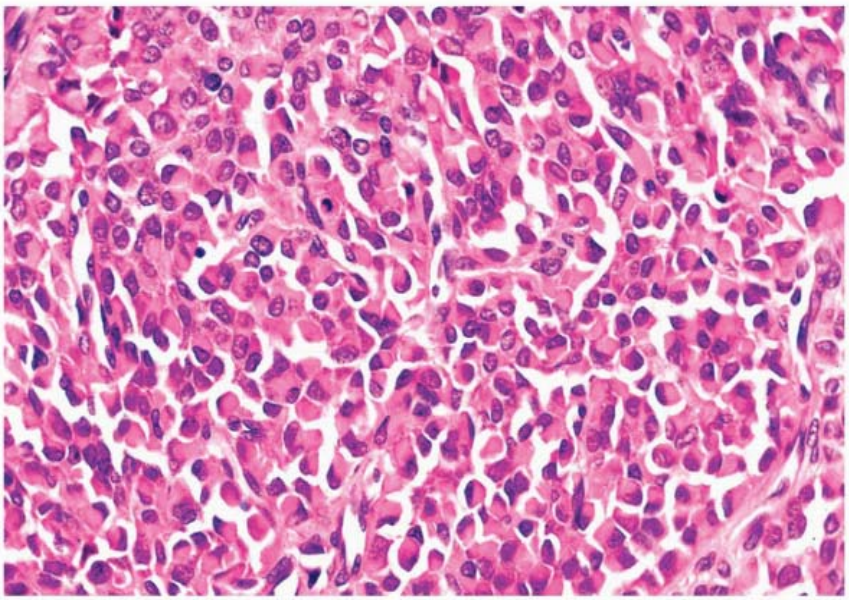


Fig 14 : Myoepithelioma plasma cell type (HE X 100)

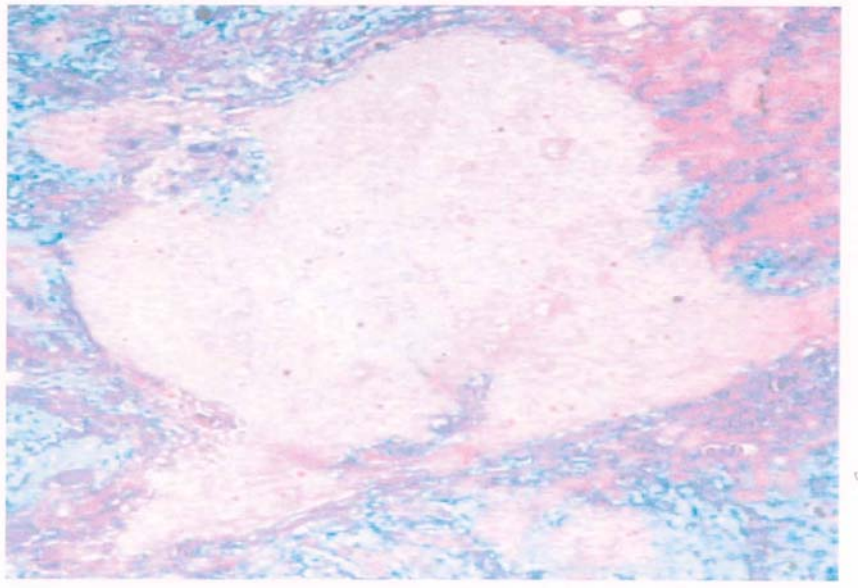


Fig 15 : Pleomorphic adenoma (Alcian blue X100)

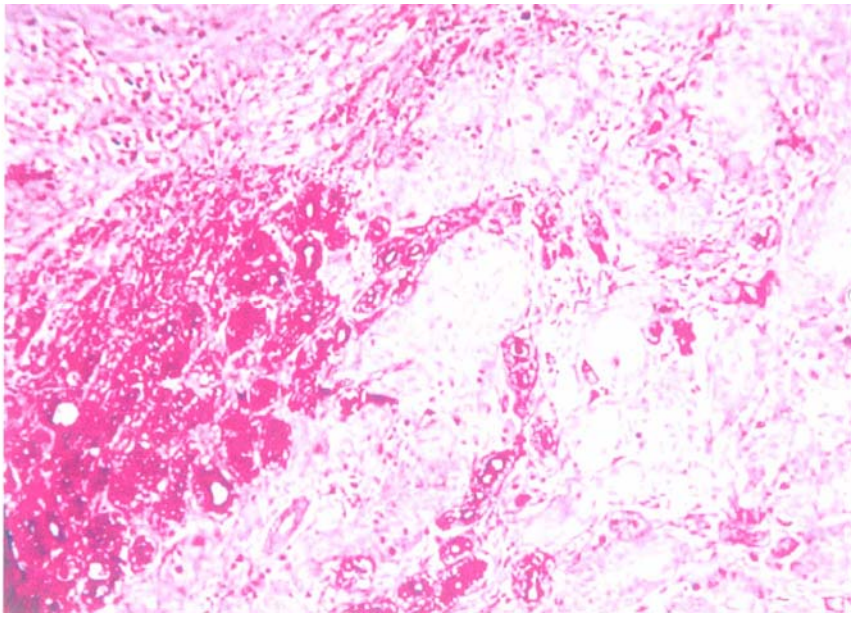


Fig 16 : Mucoepidermoid carcinoma (PAS X 100)

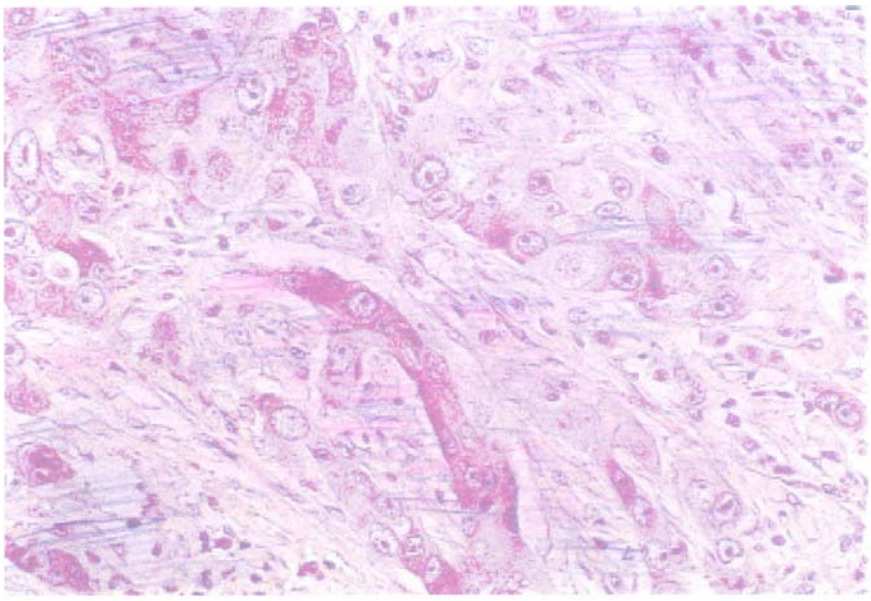


Fig 17 : Oncocytic carcinoma (PTAH X 400)

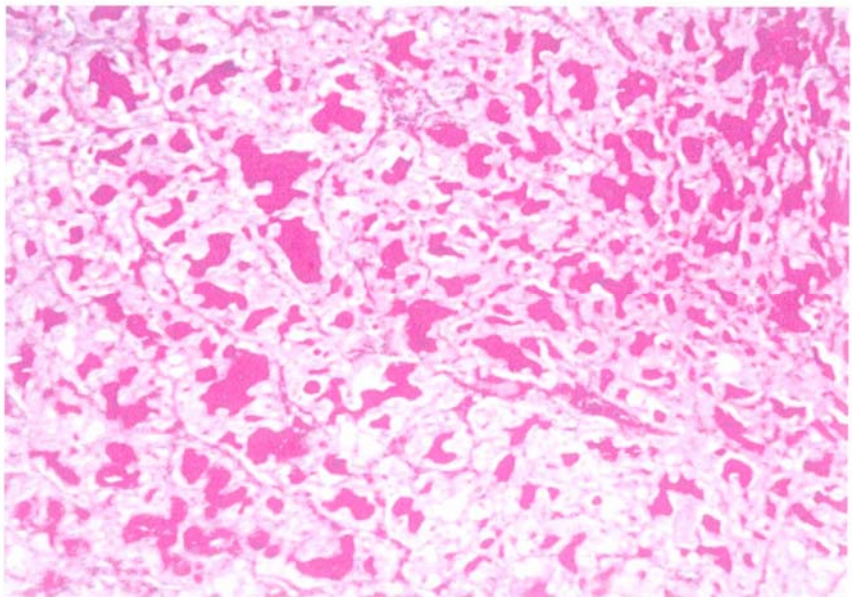


Fig 18 : Acinic cell Tumour (PAS X 40)

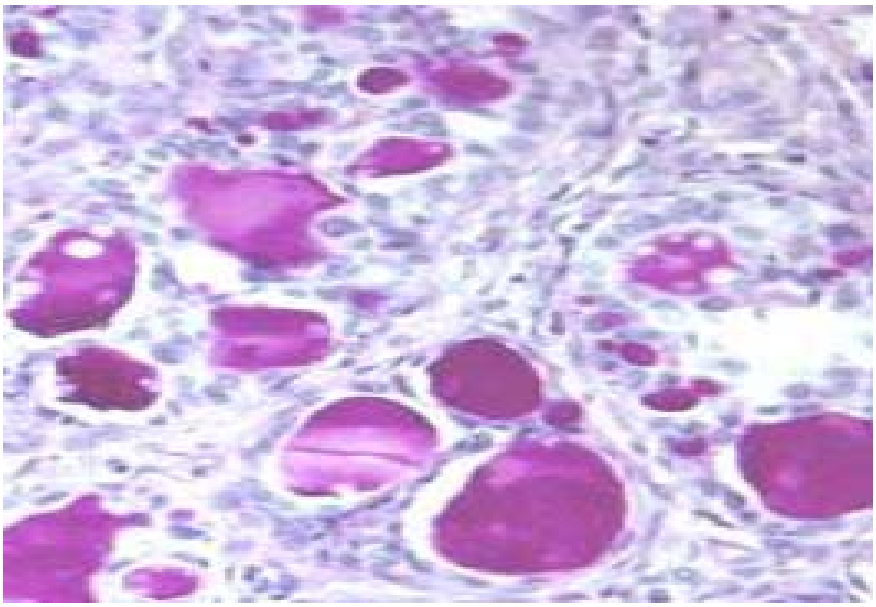


Fig 19 : Adenoid Cystic Carcinoma (PAS-100X)

DISCUSSION

This study broadly analyzed the pattern of salivary gland lesions presented to this tertiary care center over a period of 5 years from 2006 to 2010. The lesions were classified into non-neoplastic and neoplastic and correlation was done with the demographic data collected along with the biopsy request .

Type of lesions

Neoplastic lesions were more common than non-neoplastic lesions. We had 63 (78.75%) neoplastic lesions and 17 (21.25%) non-neoplastic lesions. This observation is similar to that of Jeyaram et al loc.cit (2001) where they have recorded neoplasm in 74.5% of their cases and the non-neoplastic lesions contributed to 25.5%. A similar study from eastern part of India by Bandhopadhyay et al loc.cit (2005) had reported 53.4% of salivary gland neoplasam and 40.5% of non-neoplastic lesions.

Age

The mean age of presentation of the salivary gland lesions was seen at fourth decade of life. The mean age was 41.9 in our study. This is almost similar to the observation of Nagarkar et al loc.cit (2004) and Jeyaram et al loc.cit(2001).

Gender

In our study we had a total of 54 (67.5%) female patients and 26 (32.5%) male patients. This is very similar to the data reported in the literature that lesions of the salivary gland are more common in women

gender. Our data correlates very well with the data of Ansari et al (2007) who had observed lesion in 60% of women and men contributed to 40%. The data was also very similar to that of de Oliveira et al (2009) study in which females were 61% and men 39%.

In few studies like that of Ladeinde et al (2007) men outnumbered women . A similar observation was given by Li et al (2008) who observed 53.5% lesion in men and the rest 46.5% in women.

Our results correlated with the observations of authors like Musani et al (2008) and Satko et al (2000).

Analysis of non- neoplastic lesions

We had a total of 17 cases with diagnosis of non-neoplastic conditions. The most common of them was sialadenitis (16 cases) and a single case with sialolithiasis. Again a female preponderance of the lesions were observed with 11 female patients to 6 male patients.

Sialadenitis

Analysis of the cases with sialadenitis, the most common pattern was that of chronic non specific sialadenitis with mild lymphocytic infiltration of the acinar structures of major salivary gland. The other more consistent observations were parenchymal atrophy, which we saw in 10 of our cases, similar to the observation of Harrison et al (1997) and we had fibrosis in 2 of our cases akin to the findings of Kurashima et al (1986).

Seifert G (1997) found that most of the cases reported on chronic sialadenitis have a high statistical association with rheumatoid arthritis and he attributed an immunological cause for that.

Out of the 16 cases, we had significant history of rheumatoid arthritis in 5 cases, of which one had positivity for serum Rheumatoid Arthritis factor(RA factor).

Further sub typing of the lesions reported as chronic sialadenitis, we had a single case of chronic granulomatous sialadenitis and another case of chronic xantho –granulomatous sialadenitis. The most common causes attributed to the granulomatous tissue response are tuberculosis, sarcoidosis, duct obstruction due to calculi and extravasation of mucin in tumors. In both of our case we did not find any specific etiological factor attributed towards granuloma.

Sialolithiasis

According to Lutcavage et al (1991) calculi may form in the major ducts of submaxillary sublingual and parotid glands. They may be bilateral and multicenteric. In our study we had a single case present with calculi in the submadibular gland. This correlates well with the observations of Husted (1953), who found out that calculi are more common in submandibular gland as the saliva is more concentrated with calcium salts. Microscopically there was dilation of the duct with moderate chronic inflammation and a foci with squamous metaplasia.

Analysis of neoplastic lesions

Benign tumors

We had 50 cases (79.3%) of benign salivary gland tumors out of total 63 cases, which correlates very well with the literature that in salivary glands benign tumor out number malignant.

Pleomorphic adenoma

Of the total benign tumors, the most common was pleomorphic adenoma 42 cases (84%). It contributed 84% of total benign tumor and 52.5% of all salivary gland tumors. This observation correlates well with that of Seifert et al (1986) and Spiro RH (1986) who observed a percentage varying from 45-74%. Another study from AFIP states that the pleomorphic adenoma accounts for more than 78% of all the benign tumors of salivary gland which is very close to our study, Woods JE et al (1975).

The most common site of presentation was the parotid gland. Out of the total 42 cases 30 was located in the parotid (71.4%), followed by submandibular gland 7 case (16.6%) and the rest were from intraoral minor salivary glands. This is very similar to the observation of the Waldron et al (1988).

Regarding the age distribution more than 50% of our cases occurred under the age of 50 (31 case out of 42). Eveson et al (1985) had a similar observation in which the mean age of the patients was 43. Regarding the location of the tumor, in most of our cases the tumors was located in the lower pole of the superficial lobe of the gland. None of our

cases presented with facial paralysis. The cut surface of the mass was generally homogenous, tan to white and in four case, tiny foci of hemorrhagic area were seen probably due to fine needle aspiration cytology and in 2 cases abundant myxoid areas were seen grossly.

Out of the 42 cases reported as pleomorphic adenoma , we had 10 cases with predominant myxoid component and 4 cases with epithelium predominant areas. This is very similar to the observations of Seifert G et al (1986), who found that 12-15% of pleomorphic adenomas have epithelial component that constitutes more than 80% of the tumor. The epithelial cell component was predominates cuboidal with few cases showing spindle cells and basaloid cells. The mesenchymal element was mostly myxoid and hyaline with chondroid areas. We had 2 cases with focal osseous areas.

Myoepithelioma

Regarding other benign tumors we had a two cases of myoepithelioma, which was categorized into the plasmacytoid variant and spindle cell variant respectively. Both the lesions were from the parotid gland. The spindle cell variant was cellular with minimal stromal component whereas the plasmacytoid variant was less cellular with loosely cohesive plasmacytoid cells in a mucoid stroma. This case also had remarkable cystic degeneration .

Warthin's tumor

Warthin's tumor was reported in 2 of our cases, consisting 2.5% of the salivary gland tumors. This value is below the observation of Spiro et al loc.cit (1986) who found 4 to 11.2% incidence in their series. Both the cases occurred in parotid salivary gland. The usual male/female ratio is 26:1 Li WY and Liu HC (1987), 5:1 Chaudry AP and Gorlin R (1958). But we had a young women presenting with a cystic lesion of parotid, which turned out to be a case of warthin's tumor. Recent studies claim a marked reduction in the male predilection to 1.1:1 and 1.6:1, Lamelas J et al (1987). In both, the clinical feature was a painless fluctuant swelling in the parotid.

Basal cell adenoma

We had a single case of basal cell adenoma in a 65 year old female patient. It constituted 2% of total benign tumor and 1.2% of all salivary gland tumors in our study. This is equivalent to the observation of Ellis GL et al(1996), who recorded an incidence of 1% to 4% of all primary salivary gland tumor. It has been recorded that they predominantly (more then 75%) occur in the parotids and is common in elderly women. In our study the patient was an elderly female with a small nodule is the parotid. The tumor was composed of uniform small cells with pale eosinophilic cytoplasm and uniform round to oval nuclei. Our case was categorized into the solid variant of basal cell adenoma.

Canalicular adenoma

We had a single case of canalicular adenoma reported in a 37 year old female patient presenting with a parotid nodule. Canalicular adenoma is usually seen in minor salivary glands and they constitute 4-6% of all tumors of minors salivary gland, Waldron et al loc.cit (1988). It usually occurs in elderly women with peak incidence in the seventh decade of life. It is uncommon in patients under 50 years. But in our study we had a younger patient presenting as canalicular adenoma in a major salivary gland. We had 2 cases of benign lymphoepithelial cysts of the parotid gland. Ellis GL and Auclair PL (1996) have reported an incidence of 2-3% of all parotid surgical specimens. In our study it contributed to 2.5% of the total cases.

The diagnosis was established by the presence of dense lymphoid tissue with conspicuous germinal centers in the wall of the cyst.

Malignant tumors

We had 13 cases of malignant lesions of salivary gland reported. We had 3 cases of mucoepidermoid carcinoma and 3 cases of acinic cell carcinoma (Ref. Table – 1).

Mucoepidermoid carcinoma

Mucoepidermoid carcinoma is the most common malignant salivary gland tumor. It represents about 22 % of the malignant tumors of major salivary gland, Spiro RH et at (1978). In our series, it contributes to 23% of all malignant tumors. All of them occurred in parotid with female

preponderance. In all the three it present as a solitary painless mass of the parotid . Microscopically the tumor consist of mucous, epidermoid, intermediate, columnar and clean cells in both solid and cystic configurations. In most of the cases the mucus cells comprise less than 10%. One of our case had intraluminal papillary proliferation of the mucus cells. A similar observation was made by Auclair PL et al (1992).

Mucoepidermoid carcinoma are divided into low, intermediate and high grade types on the basis of morphologic and cytologic features. The histological features that are most useful in predicting high grade, aggressive behavior includes intracystic component less that 20%, high mitotic activity, presence of neural invasion, necrosis and cellular anaplasia, Auclair PL et al loc.cit (1992) . One of our case was categorized on high grade mucoepidermoid carcinoma due to predominance of the epidermoid component with marked cellular anaplasia. The other two cases were categorized as low grade tumor.

Acinic cell carcinoma

These are group of malignant salivary gland tumor in which the neoplastic cells demonstrates serous acinar cell differentiation. Spiro RH (1986) loc.cit had found an incidence of 10% of the primary malignant tumors. In our study, the incidences are slightly higher to around 23% and this could be due to the smaller sample size of lesions. All the 3 cases of acinic cell carcinoma occurred in the parotid region akin to the observations of Spiro RH loc.cit (1986) who found more there 80% of these tumors occur in parotids. It is a female predominant tumor and the mean age is 44 years. In our study it was more common in women and we had a single case presenting in a male patient. The mean age of the patients in our study was 51. It was a slow growing mass and one of our case experienced facial muscle weakness. Ellis GL and Corio RL (1983) have reported a facial muscle weakness in 5-10% of their patients.

Regarding the histoarchitecture, 2 of our cases presented with predominant solid pattern and we had a single case with microcystic pattern. This microcystic pattern of acinic cell tumor occurred in a young lady 28 year old presenting with a nodule in parotid.

Adenocarcinoma (NOS)

Salivary gland adenocarcinoma (NOS) fails to exhibit prominence of any of the histomorphological features that characterise the more specific carcinoma types. Auclair PL and Ellis GL (1991) have reported an incidence of 8.8% and 44.7% of all malignant tumors. In our series it

contributed 15.3% of all malignant salivary gland tumors. Both the cases presented with mass in the parotid region. One of them presented with facial muscle weakness.

Microscopically it is composed of a heterogeneous, glandular, duct like and infiltrative growth pattern.

These tumors are categorized into low grade, intermediate and high grade tumors based on the formation of ductal and tubular structures, mitotic activity and nuclear features. Both of our cases were included on high grade adenocarcinoma (NOS) .

Adenoid cystic carcinoma

Adenoid cystic carcinoma is a malignant neoplasm of the salivary ducts and myoepithelial cells. Ellis GL and Auclair PL loc.cit (1996) have reported an incidence of 7.5% of malignant salivary gland tumor. In our study it constituted 7.6% of the total malignant salivary gland tumors.

The case from our series was a young 33 year old lady presenting with a gradually increasing mass of the submandibular region. The mass presented with pain and tenderness. Histologically the tumor showed a cribriform pattern of interconnecting cords and nests of tumor cells surrounding small cyst like structures of variable size filled with basophilic and hyalinised eosinophilic material.

Malignant oncocytoma

They represent less than 1% of all salivary gland tumors, Ellis GL and Auclair PL loc.cit (1996). We had a single case of malignant oncocytoma constituting 1.58% of the total tumor cases.

Goode RK and Corio RL (1988) have reported a predominance of this tumors in the parotid gland. In our study the tumor was seen in th submandibular gland in an elderly woman.

Microscopically the tumor was composed of large round to polyhedral cells arranged in sheets and island with finely granular eosinophilic cytoplasm and moderately pleomorphic nuclei.

Adenosquamous carcinoma

It is a rare neoplasm that simultaneously demonstrates carcinoma of the surface epithelium and salivary gland type adenocarcinoma. Genighty et al (1968) have described the most common sites of the tumor as posterior tongue, tonsillar pillars and floor of mouth. We had a single case of adenosquamous carcinoma of the parotid, presenting as a nodular mass in the parotid with surface ulceration. The lesion was painful. The superficial pattern of the tumor was squamous cell carcinoma and the deeper was that of adenocarcinoma. The zone of transition from squamous carcinoma to adenocarcinoma is usually evident. The tumor infiltrates and invades adjacent tissues.

Squamous cell carcinoma

Diagnosis of primary squamous cell carcinoma requires inclusion of primary disease in some other site, particularly the head and neck. Schneider AB et al (1977) had reported an incidence of 0.9% to 4.7%. In our series, we had a single case of primary squamous cell carcinoma contributes to 1.58% of total salivary gland tumors.

Shemen LJ and Huvos AG (1987) have reported a mean age of 64 years. In our study the patient was a female 60 years old with a parotid mass.

Microscopically the tumors are mostly keratinizing squamous cell carcinomas and special stains do not disclose any intracytoplasmic mucin.

Epithelial-Myoepithelial carcinoma

This is a biphasic neoplasm of duct and myoepithelial cells. They are now recognized as low-grade adenocarcinoma, Thackray AC and Lucas RB (1974).

Vanderwal JE et al (1998) have reported as average incidence of 1% of salivary gland neoplasm. In our series it constitutes 1.5% of total salivary gland tumors. The predominant site of involvement is the parotid, Batsakis et al (1992).

In our study the tumor occurred in the submandibular salivary gland.

The characteristic histomorphology is a biphasic cellular pattern of ductal elements composed of cuboidal cells surrounded by large clear staining myoepithelial cells.

Incidence of salivary gland tumors reported from various countries

S.No.	Author	Country/State	Sex		Tumor type	
			Male %	Female %	Benign %	Malignant %
1.	Satko et al (2000)	Slovakia	47.41	52.59	74	26
2.	Jayaram & Dashini (2001)	Malaysia	<50	>50	71.4	25.77
3.	Gill et al. (2001)	Pakistan	65.7	34.3	-	-
4.	Kolude et al. (2001)	Nigeria	46.51	53.49	49.9	50.1
5.	Nagarkar et al. (2004)	Chandigarh	-	-	75	25
6.	Lima et al.(2005)	Portuguese	<50	>50	76.33	23.67
7.	Bandyo padhyal et al. (2005)	West Bengal	-	-	81.84	18.16
8.	Ansari (2007)	Iran	40	60	68.4	31.6
9.	Ladeinde et al. (2007)	Nigeria	52.38	47.62	39.2	60.8
10.	Subhashraj (2008)	Pondicherry	-	-	62	38
11.	Li et al. (2008)	China	53.5	46.5	-	-
12.	Musani et al. (2008)	Pakistan	42.65	57.35	74.5	25.5
13.	De oliveira et al. (2009)	Brazil	39	61	78.3	21.7
14.	Dhanuthai et al. (2009)	Thailand	42.02	57.98	47.2	52.7
15.	Wierzbicka et al. (2010)	Poland	-	-	86.76	13.23

SUMMARY AND CONCLUSION

This study analyzed the incidence and distribution of salivary gland lesions over a period of 5 years from the specimen submitted to the pathology department of Tirunelveli Medical College during the period between 2006 to 2010.

Distribution of lesions recorded were neoplasm 78.75%, sialadenitis 20% and sialolithasis 1.25%. Lesions occurred from 10 years to 80 years of age with the mean age of 41.19. There is predominance of lesions in females than males was seen. Parotid gland was mostly affected followed by submandibular gland.

Tumour was recorded from 10 to 80 years of age and 76.19% of tumours occurred at the age group of 20 to 60 years. Most of the benign tumour was seen in the second and third decades while malignant was in fifth decade of life. Females were mostly affected then males. Most tumours were in the parotid gland followed by submandibular gland. Most common benign tumour was pleomorphic adenoma while malignant tumour was mucoepidermoid carcinoma and acinic cell carcinoma.

Sialadenitis was most common non neoplastic lesion and seen between 15 to 56 years of age. It was seen mostly in females then males. Submandibular gland was mostly affected followed by parotid gland.

Analysis of the lesions showed statistically significant difference in age, sex, site distribution except submandibular sialadenitis and age distribution of malignant tumour.

MASTER CHART

S.No	OP/IP No.	M/F	Age	Neoplasm / Nonneoplasm	Non neoplastic Condition	Benign/ Malignant	Neoplasm type	Organ affected
1	59/06	F	45	Neoplasm	-	Benign	Pleomorphic adenoma	Parotid
2	199/06	F	28	Neoplasm	-	Benign	Pleomorphic adenoma	Parotid
3	202/06	F	37	Neoplasm	-	Benign	Monomorphic adenoma	Parotid
4	267/06	F	33	Non neoplasm	Sialadenitis	-	-	Submandibular gland
5	310/06	F	50	Neoplasm	-	Benign	Pleomorphic adenoma	Parotid
6	439/06	F	38	Non neoplasm	sialadenitis	-	-	Parotid
7	695/06	F	39	Neoplasm	-		Pleomorphic adenoma	Parotid
8	819/06	F	10	Neoplasm		-	Pleomorphic adenoma	Submandibular gland
9	946/06	M	16	Neoplasm	-		Pleomorphic adenoma	Accessary salivary gland
10	1061/06	M	37	Neoplasm		Benign	Mixed parotid tumour	Parotid
11	1126/06	F	55	Neoplasm		Benign	Pleomorphic adenoma	Parotid
12	1144/06	M	26	Neoplasm			Pleomorphic adenoma	Parotid
13	1223/06	F	45	Neoplasm			Pleomorphic adenoma	Parotid
14	1365/06	F	55	Non neoplasm	Sialadenitis		-	Submandi bular gland
15	1448/06	F	42	Non neoplasm	Sialadenitis		-	Submendibular gland
16	234/07	F	24	Neoplastic		Malignant	Mucoepidermoid carcinomra	Parotid
17	307/07	F	48	Neoplasm		Benign	cpleomorphic adenoma	Parotid
18	32/07	F	55	Neoplasm		Benign	Pleomorphic adenoma	Parotid

19	659/07	F	36	Neoplasm		Malignant	Adenosquamous carcinoma	Parotid
20	720/07	M	80	Neoplasm		Benign	Pleomorphic adenoma	Parotid
21	804/07	F	40	Neoplasm		Benign	Pleomorphic adenoma	Submandibular gland
22	924/07	M	60	Neoplasm		Benign	Warthin's tumour	Submandibular gland
23	1063/07	M	38	Neoplasm			Pleomorphic adenome	Parotid
24	1080/07	F	20	Neoplasm			Pleomorphic adenoma	Parotid
25	1119/07	M	39	Neoplasm			Pleomorphic adenoma	Parotid
26	1439/07	F	50	Neoplasm		Malignant	Adenocarcinoma	Parotid
27	1442/07	M	50	Neoplasm		Benign	Pleomorphic adenoma	Parotid
28	1492/07	F	25	Neoplasm		Benign	Warthin's tumour	Parotid
29	1626/07	M	73	Neoplasm		Benign	Pleomorphic adenoma	Parotid
30	79/08	M	39	Nonneoplasm	Sialadenitis	-	-	Submandibular gland
31	204/08	M	40	Non neoplasm	Sialadentis		-	Submandibular gland
32	317/08	F	48	Nonneoplams	Sialolithiasis		-	Submandibular gland
33	331/08	F	35	Neonneoplams	-		Pleomorphic adenoma	Parotid
34	383/08	M	17	Neoplasm	-		Pleomorphic adenoma	Submandibular gland
35	394/08	F	30	Neoplasm	-	Benign	Pleomorphic adenoma	Parotid
36	471/08	F	28	Neoplasm		Benign	Pleomorphic adenoma	Parotid
37	546/08	F	45	Neoplasm		Benign	Pleomorphic adenoma	Parotid
38	628/08	M	65	Neoplasm			Pleomorphic adenoma	Parotid
39	802/08	F	40	Neoplasm			Pleomorphic adenoma	Parotid
40	907/08	F	48	Neoplasm			Pleomorphic adenoma	Parotid
41	1041/08	F	32	Neoplasm			Pleomorphic adenoma	Parotid
42	1150/08	F	40	Neoplasm		Malignant	Mucoepidermoid	Parotid

							carcinoma	
43	1216/08	M	56	Non neoplasm	Chronic sialadenitis	-	-	Submandibular gland
44	1221/08	F	38	Non neoplasm	Chronic sialadenitis	-	-	Parotid
45	1420/08	F	65	Neoplasm			Pleomorphic adenoma	Parotid
46	1466/08	F	28	Neoplasm	-	Malignant	Acinic cell carcinoma	Parotid
47	1487/08	M	54	Neoplasm		Benign	Pleomorphic adenoma	Sublingual gland
48	1558/08	M	40	Neoplasm	Chronic sialadenitis		-	Submandibular gland
49	1596/09	M	70	Neoplasm	-	Benign	Pleomorphic adenoma	Parotid
50	2180/09	F	23	Neoplasm			Pleomorphic adenoma	Parotid
51	2202/09	F	40	Neoplasm		Malignant	Epithelial – Myoepithelial carcinoma	Submandibular gland
52	2401/09	F	65	Nonneoplanm		Benign	Basal cell adenoma	Parotid
53	147/09	F	45		Chronic sialadenitis		-	Submandibular gland
54	170/09	F	36	Neoplasm	-	Benign	Pleomorphic adenoma	Parotid
55	2449/09	M	65	Neoplasm		Malignant	Mucoepidermoid tumour	Parotid
56	393/09	F	26	Neoplasm		Benign	Benign lymphoepithelial cyst	Parotid
57	526/09	M	45	Neoplasm		Benign	Myoepithelioma with cystic degeneration	Parotid
58	584/09	F	55	Neoplasm		Benigns Malignant	Benign mixed tumour & high grade adenocercinoma	Parotid
59	608/09	M	27			Benign	pleomorphicadenoma	Parotid
60	619/09	F	52	Nonneoplasm	Chronic sialadenitis	-		Submandibular gland

61	1032/09	F	33	Neoplasm		Malignant	Adenoid cystic carcinoma	Submandibulan gland
62	1213/09	M	20	Non neoplasm	Chronic sialadenitis	-	-	Submandibulan gland
63	1214/09	F	50	Neoplasm		Malignant	Acinic cell tumor	Parotid
64	1252/09	F	15	Non neoplasm	Sialadenitis			Parotid
65	1371/09	M	40	Neoplasm		Benign	Pleomorphic adenoma	Hard palate
66	4/10	F	73	Neoplasm		Malignant	Malignant Oncocytoma	Submandibular gland
67	185/10	F	60	Neoplasm		Benign	Pleomorphic adenoma	Parotid
68	326/10	F	24	Neoplasm			Pleomorphic adenoma	Submandibular gland
69	507/10	M	34	Neoplasm			Pleomorphic adenoma	Parotid
70	1807/10	F	23	Neoplasm		Benign	Pleomorphic adenoma	Submandibular gland
71	553/10	M	76	Neoplasm		Malignant	Acinic cell tumour	Parotid
72	567/10	F	29	Nonneoplasm	Chronic sialadenitis		-	Submandibular gland
73	658/10	F	36	Nonneoplasm	Chronic sialadenitis		-	Parotid
74	707/10	M	30	Nonneoplasm	Chronic sialadenitis		-	Parotid
75	922/10	F	25	Neoplasm	-	Benign	Pleomorphic adenoma	Parotid
76	976/10	F	60	Neoplasm		Malignant	Well differentiated squamous cell carcinoma	Parotid
77	981/10	F	35	Neoplasm			Pleomorphic adenoma	Parotid
78	984/10	M	42	Neoplasm			Pleomorphic adenoma	Parotid
79	1391/10	F	34	Neoplasm		Benign	Myoepithelioma	Parotid
80	1405/10	F	25	Neoplasm		Benign	Benign lymphoepithelial cyst	Parotid

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